American Journal of Diseases of Children

VOLUME 67 · MARCH 1944 · NUMBER 3

COPYRIGHT, 1944, BY THE AMERICAN MEDICAL ASSOCIATION

DEVELOPMENT AND GROWTH OF THE HUMAN EMBRYO AND FETUS

A GRAPHIC REPRESENTATION OF SOME ASPECTS

H. WILLIAM CLATWORTHY JR., M.D., AND ROBIN G. ANDERSON, M.D.

BOSTON

The available literature on human development does not contain in an accessible and compact form the data necessary for the study of the relationship between the rate of growth and the differentiation of the various organs of the human embryo and fetus. This communication does not include original data but is, rather, a graphic composition designed to bring together in comparable form information obtained from the literature pertaining to the relationship of rate of growth to structural changes in human prenatal development. There has been no attempt to interpret the material presented. We have had two purposes in mind: first, to make data pertaining to growth and development of various organs readily available, and, second, to correlate as completely as possible the rates of growth and the morphologic changes of these organs. A chart is presented for each of the following structures: head, spinal cord, thyroid gland, thymus, heart, lung, alimentary canal including stomach, stomach alone, liver, pancreas, spleen, kidney and adrenal gland.

CONSTRUCTION OF THE CHARTS

The legend for each chart contains a list of the pertinent structural changes arranged chronologically. The chart itself contains two curves, one showing the rate of growth of a given organ relative to the rate of growth of the whole fetus as measured in percentage of total body volume and the other showing the weight of the organ in grams. Both are plotted against fetal age. Data in the literature based on menstrual age have been converted to fetal age.

The rate of growth is indicated by the slope of the solid line curve, which was obtained by plotting the per cent of the body volume attained by a given structure against the fetal age. Thus, when the curve is rising the per cent of body volume occupied by the structure is increasing, and the organ therefore must be growing at a rate greater than that of the embryo as a whole. The reverse is true in the event of a falling curve. The percentages of body volume of the various organs at various periods before birth have been obtained directly from the work of C. M. Jackson [1] and calculated from the curves in the more recent papers of R. E. Scammon [2] and of Scammon and Kittelson.[3]

The broken line curve represents the weight in grams of a given organ. It is made by taking the per cent of the body volume at a given fetal age, assuming it to be essentially equal to the per cent of the body weight,[1] and multiplying it by the total weight of the embryo at that age as calculated from G. L. Streeter's graphs.[4]

It should be emphasized that the importance of the curves showing the rate of growth lies not in the specific values charted but in the general shape. Therefore, we have arbitrarily adopted for our final curves a composite of Jackson's and Scammon's curves which emphasizes the most significant trends.

The curves showing the actual weights of the structures are presented to avoid the possibility of confusing the rate of growth with the true weight of the organ and, furthermore, to give an approximation of the size of any structure at any given period.

The data for the differentiations listed in the legends have been obtained from such general

From the Departments of Pathology, Harvard Medical School and The Children's Hospital.

1. Jackson, C. M.: Prenatal Growth of the Human Body: Its Organs and Parts, Am. J. Anat. **9**:119, 1909.

2. Scammon, R. E.: (*a*) Prenatal Growth and Natal Involution of Human Suprarenal Gland, Proc. Soc. Exper. Biol. & Med. **23**:809 (May) 1926; (*b*) The Growth of Various Regions of the Body in the Fetal Period, ibid. **23**:238, 1926; (*c*) The Prenatal Growth of the Human Thymus, ibid. **24**:906, 1927; (*d*) The Prenatal Growth of the Human Pancreas, ibid. **24**:391 (Feb.) 1927; (*e*) The Growth of the Human Stomach, Am. J. Dis. Child. **17**:395 (June) 1919.

3. Scammon, R. E., and Kittelson, J. A.: The Growth of the Gastro-Intestinal Tract of the Human Fetus, Proc. Soc. Exper. Biol. & Med. **24**:303 (Jan.) 1927.

4. Streeter, G. L.: Weight, Size and Age of the Human Embryo, Publication 274, Carnegie Institution of Washington, 1920.

works as those by Arey,[5] Keibel and Mall[6] and Keith.[7]

EXAMPLE

The detailed method used in deriving the various curves may be described best by presenting an outline of the procedure which was followed in constructing the chart for the thymus

TABLE 1.—*Jackson's Measurements*

Crown-Rump Length, Cm.	Estimated Menstrual Age,[4] Wk.	Per Cent of Body Volume of Individual Thymuses	Average Per Cent of Body Volume
3.1	8	0.008	0.008
7.5- 9.5	14	0.100; 0.075; 0.102	0.092
10.5-11.5	16	0.148; 0.105; 0.103	0.118
13 -14	18	0.090; 0.107; 0.243	0.147
15 -16	20	0.125; 0.117; 0.200	0.148
17 -17.5	22	0.179; 0.171	0.175
18 -20	24	0.113; 0.165; 0.232	0.170
21	26	0.221	0.221
23 -26	28	0.425; 0.256	0.340
31.5-35	38	0.311; 0.212; 0.660; 0.32	0.376

(chart 2). The steps in the construction of the final chart are represented graphically in chart 1, and the data are listed in tables 1 to 4.

A. The final curve of the rate of growth (heavy, solid line) is a composite curve derived from three sources (chart 1).

1. Jackson's[1] own measurements (table 1) of 32 embryos are represented by the broken line.

2. Jackson's[1] review of the measurements (table 2) of 800 specimens reported in the literature, plus his own, are represented by the fine, solid line.

TABLE 2.—*Measurements from Literature Reviewed by Jackson*

Menstrual Age (Lunar Months)	Number of Specimens	Per Cent of Body Volume
2	1	0.008
3	1	0.190
4	28	0.134
5	50	0.149
6	45	0.175
7	19	0.285
8	60	0.259
9	6	0.240
10	101	0.313

3. The dot-dash curve is our representation of Scammon's observations (table 3).[2c]

After conversion of all menstrual ages into fetal ages (menstrual age less 2 weeks is equal to fetal age according to Arey[5]), each of the three curves is obtained by plotting the per cent of the body volume against the fetal age. When these curves are superimposed, as in chart 1, they are observed to be similar in shape, although they present slight differences in actual point values.

The curve drawn in the heavy, solid line, chart 1, is our composite of the three separate curves; this is then used as the curve representing the rate of growth in chart 2, and the corresponding curves for charts 2 to 14 are derived in similar fashion.

TABLE 3.—*Scammon's Measurements*

Menstrual Age, Wk.	Weight of Thymus (Estimated), Gm.	Total Weight of Embryo,[4] Gm.	Per Cent of Body Weight (Assumed from % of Body Volume)
18	0.3	200	0.15
24	1.5	630	0.24
28	3.0	1,040	0.30
31	4.9	1,490	0.33
34	6.2	2,070	0.30
36	7.6	2,470	0.30
38	8.5	2,920	0.29
40	10.0	3,400	0.29

It is indeed unfortunate that the available measurements of embryos between 1 and 3 months of age are so few that we have been obliged to construct parts of these curves from what may prove later to be an inadequate series of observations. In general, however, the values calculated from data obtained from a larger series of individual specimens have been given precedence over values representing a smaller group.

TABLE 4.—*Method of Computing Weight of the Part*

Menstrual Age, Wk.	Total Weight of Embryo, Gm.	Per Cent of Body Volume	Computed Weight of Thymus, Gm.
12	14.2	0.17	0.024
14	45.0	0.14	0.063
16	108.0	0.15	0.160
18	190.0	0.17	0.323
20	316.0	0.21	0.660
22	460.0	0.25	1.15
24	630.0	0.29	1.82
26	820.0	0.30	2.46
28	1,040.0	0.29	3.02
30	1,320.0	0.31	4.0
36	2,480.0	0.29	7.2
38	2,910.0	0.28	8.1

B. The figures from which the curve for the weight in grams is plotted were obtained by multiplying the weight of the embryo at a given time as given by Streeter[4] by the per cent of body volume of the organ as ascertained from the final curve previously described (table 4). The calculated weight of the organ is then plotted against the fetal age.

5. Arey, L. B.: Developmental Anatomy, ed. 4, Philadelphia, W. B. Saunders Company, 1941.

6. Keibel, F., and Mall, E. P.: Human Embryology, Philadelphia, J. B. Lippincott Company, 1910.

7. Keith, A.: Human Embryology and Morphology, London, Edward Arnold & Co., 1933.

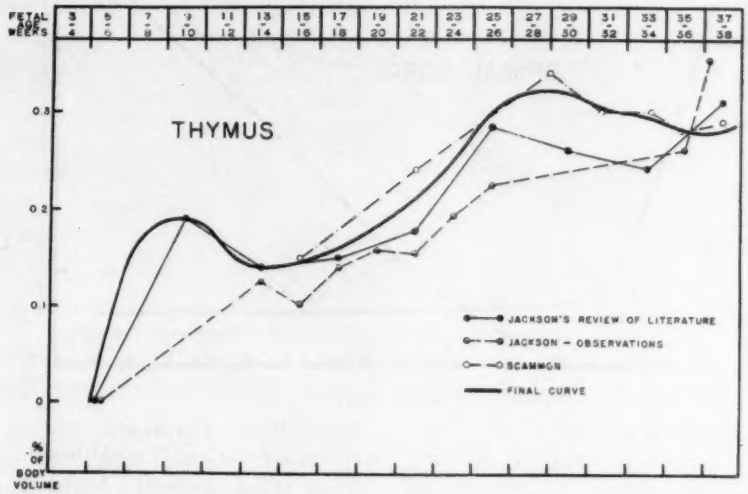

Chart 1.—Thymus. Sample chart showing the method of deriving final curves for percentage of body volume from the data.

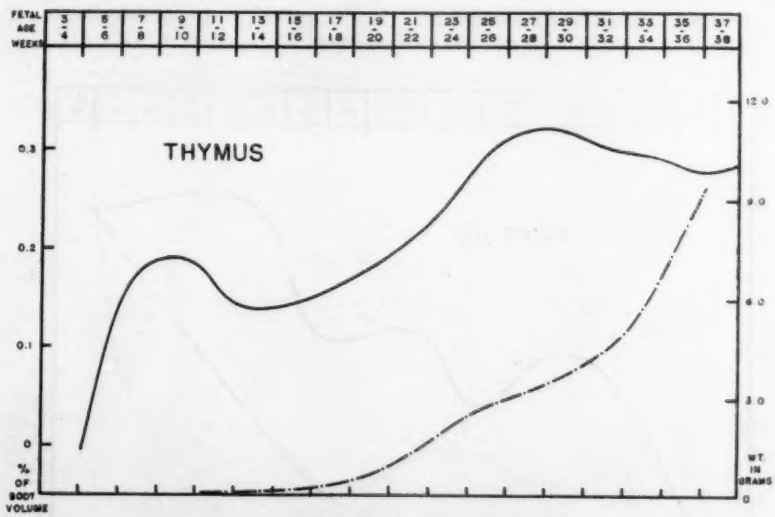

Chart 2.—Thymus.

Sixth Week: Ventral sacculations from pouch III are prominent; buds from pouch IV and cervical sinus appear, then atrophy.

Seventh Week: Thymic pockets detach; migration to superior mediastinum occurs.

Eighth Week: Lateral lobes unite; lobes solidify; remnants of pouch III disappear.

Ninth Week to Birth: Broods of lymphoid cells appear (ninth week); epithelial cells proliferate, producing syncytium (tenth week); Hassall corpuscles are recognizable (tenth week).

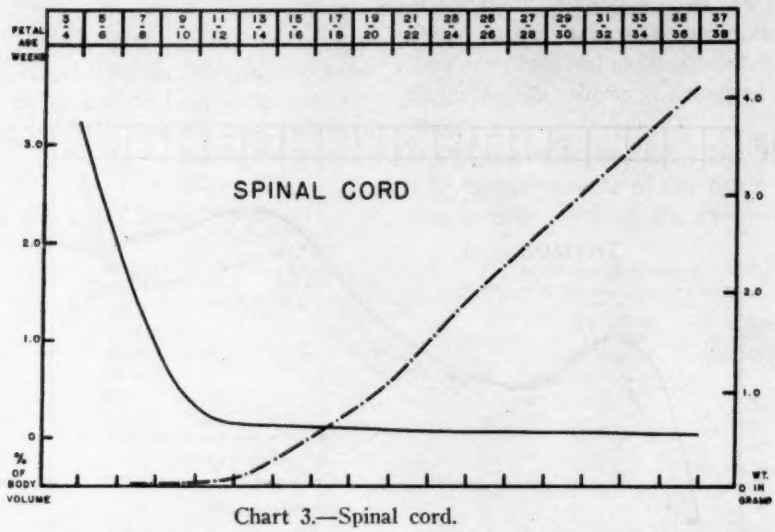

Chart 3.—Spinal cord.

Second Week: Neural plate is present.

Third Week: Neural groove is indicated; primary neural sheath forms.

Fourth Week: Neural groove begins to close; neural crests are continuous bands; white and gray areas are differentiable; anterior roots form; anterior neuropore closes.

Fifth Week: Posterior neuropore closes; neural crests segment into ganglions; anterior and posterior celiac axes form.

Sixth Week: Marginal, ependymal and mantle layers are represented; sympathetic ganglions are present.

Seventh Week: Ventral and lateral gray columns can be seen.

Eighth Week: Dorsal gray columns appear; cord and vertebral column are of equal length.

Ninth Week to Birth: Vertebral column starts to lengthen faster than cord (ninth week); columns of Goll and Burdach form, obliterating dorsal portion of the neural canal (ninth week); pial and arachnodural layers separate (ninth week); long association tracts start forming (tenth week); anterior horns are complete (eleventh week); cervical and lumbar enlargements appear (twelfth week); cauda equina and filum terminale appear (twelfth week); myelination begins (fifth month); pyramidal tracts grow down (fifth month).

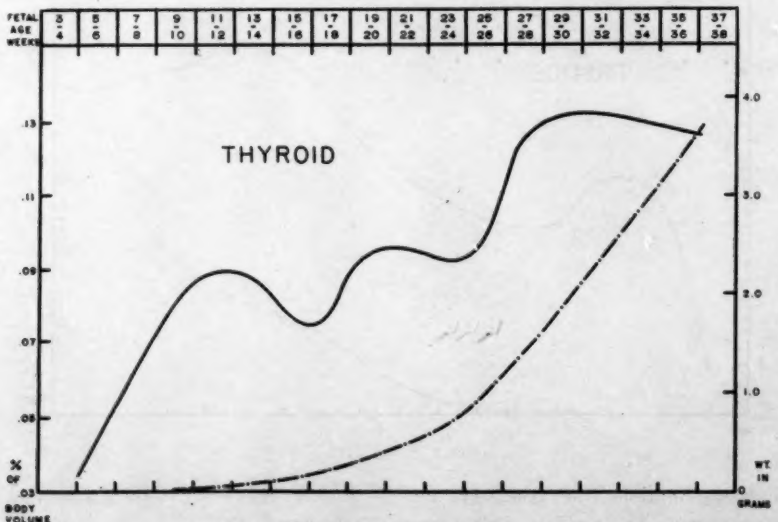

Chart 4.—Thyroid.

Third Week: Anlage appears as midventral outpouching in pharynx.

Fourth Week: Thick-walled sac forms.

Fifth Week: Stalked, bilobed sac present.

Sixth Week: Thyroglossal duct begins to fibrose; gland converted into solid epithelial plates; foramen cecum is present.

Seventh Week: Transverse plate forms; thyroglossal cord breaks up; gland becomes crescentic; foramen cecum closes; reticulated mesenchymal columns invade plates.

Eighth Week: Follicles start forming.

Third Month to Birth: Colloid appears (third month); gland is functional (third month); adult configuration attained (twelfth week).

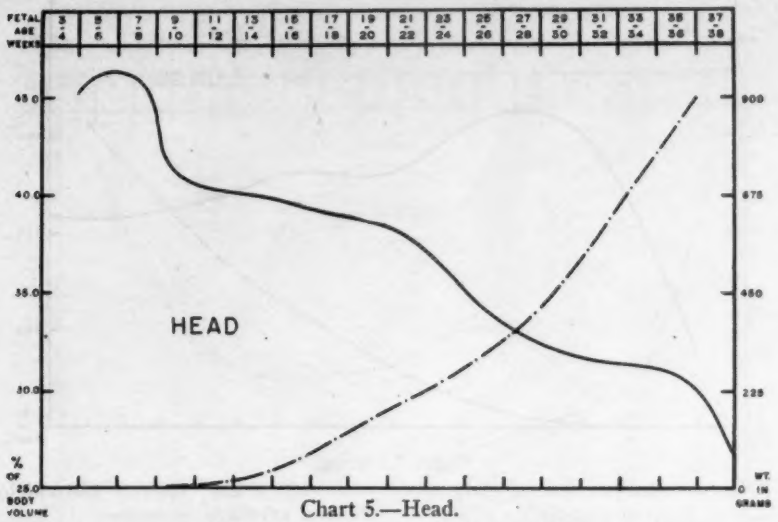

Chart 5.—Head.

Third Week: Head process curves caudally; arch I appears.

Fourth Week: Maxillary and mandibular processes are prominent; olfactory placode is present; mandibular processes unite.

Fifth Week: Frontonasal process differentiates; arch II covers arches III and IV to form cervical sinus; olfactory pits still open; branchial arches are completed.

Sixth Week: Part of external auditory meatus develops from groove I; lateral nasal and maxillary processes fuse; cervical sinus deepens; labiodental laminas appear.

Seventh Week: Frontonasal and maxillary processes fuse; ossification begins in mandible; frontal and parietal bones are membranous; interparietal squamosal and palatine bones are present; branchial arches are no longer visible.

Eighth Week: Frontal, parietal, interparietal, squamosal and palatine bones begin to ossify; epithelium in nose proliferates; superior maxillary, nasal and lacrimal bones and vomer begin to ossify.

Ninth Week to Birth: Hard palate fuses (fifth week to fourth month); pinna assumes definite form (tenth to fourteenth week); ossification begins in premaxillary, temporal, occipital and sphenoid bones (eleventh and twelfth weeks); nasal septum and palate fuse (eleventh to twelfth week); accessory nasal sinuses develop (thirteenth week); sebaceous glands are present (fifth month); turbinate bones form (sixth month); accessory sinuses are present but rudimentary (tenth month).

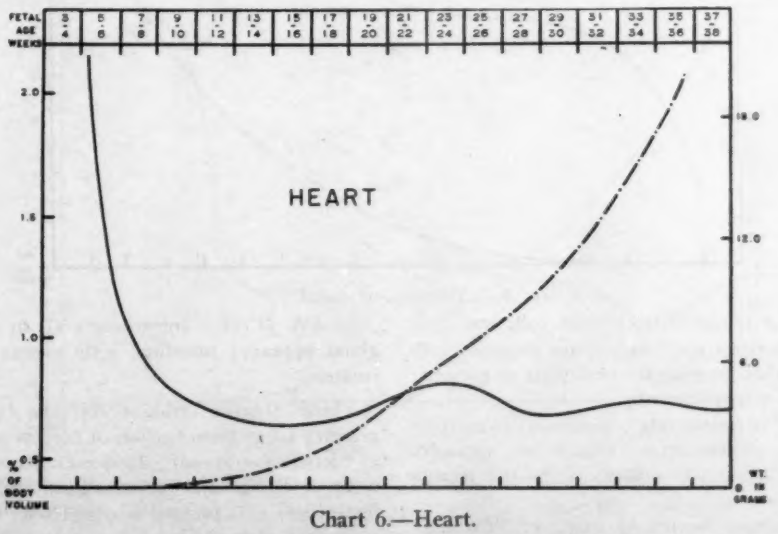

Chart 6.—Heart.

Fourth Week: Pericardial space forms; cardiac tubes fuse; cardiac tubes pulsate; dorsal mesocardium degenerates; four divisions are present (sinus venosus, atrium, ventricle and bulbus).

Fifth Week: Tube bends to "S"; anlage of septum I appears; bulbar ridges form; endocardial cushions form; atrium sacculates.

Sixth Week: Intertubal wall disappears; septum I fuses with cushions; ostium I forms; septum II appears; bulbus is divided completely; anlages of aortic, pulmonary and atrioventricular valves are present; coronary and caval valves are functional.

Seventh Week: Atrium absorbs sinus; left duct of Cuvier becomes coronary sinus; septum spurium begins to form; foramen ovale is present in septum I.

Eighth Week: Interventricular septum closes; adult configuration is established; atrioventricular bundle appears.

Ninth Week to Birth: Macroscopic and histologic differentiation continues; heart musculature becomes condensed (sixteenth week).

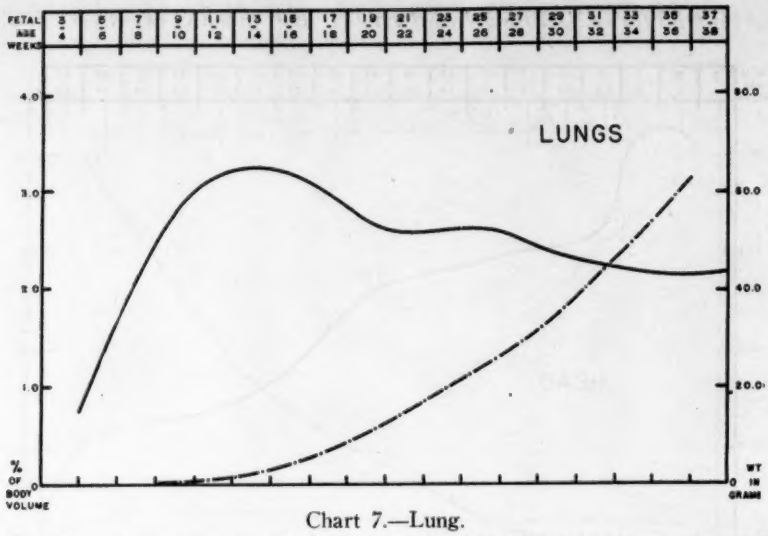

Chart 7.—Lung.

Fourth Week: Primitive pharynx forms; laryngotracheal groove forms on floor of pharynx.

Fifth Week: Tracheal and paired lung buds are prominent; lung buds acquire branches, three right and two left.

Sixth Week: Pulmonary artery branches to each bud; pulmonary lobes are definite; bronchus to each lobe is present.

Seventh Week: Larynx and epiglottis are outlined; tracheal cartilage is present.

Eighth Week: Larynx chondrifies; bronchioles branch regularly; lung is glandlike.

Third Month to Birth: Mesoderm infiltrates branching buds (third month); adult configuration is attained (third month); high cuboidal epithelium is present in trachea (third month); tracheal glands are present (fourth month); alveoli are developing (sixth month).

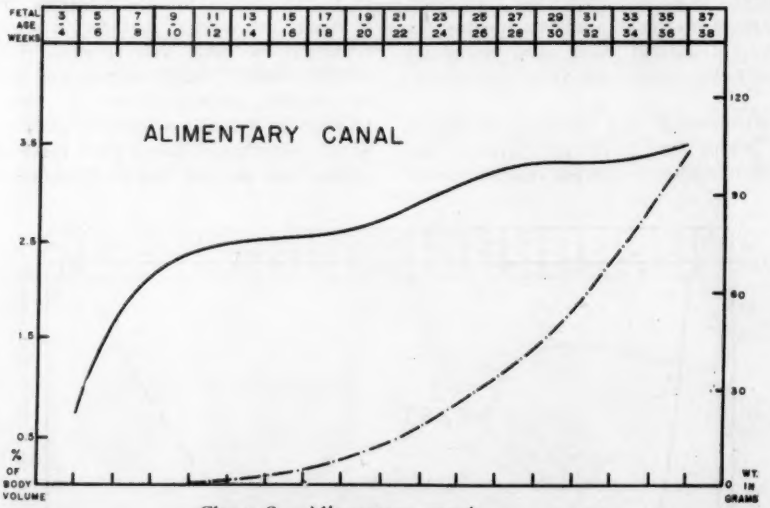

Chart 8.—Alimentary canal.

Third Week: Gut is not distinct from yolk sac.

Fourth Week: Foregut and hindgut are present; yolk sac is broadly attached to midgut; oral plate is present; esophagus is short and sphincteric.

Fifth Week: Gut is simple tube; esophagus elongates; ventral mesentery degenerates; anlage of appendix appears; tailgut is maximal; anlage of cloacal septum is present.

Sixth Week: Tongue begins to fuse; vitelline duct shrivels; oral plate ruptures; submaxillary and parotid glands are present; torsion and ventral flexion of intestine takes place; duodenal epithelium proliferates; cecum is prominent; rectal orifice moves caudally on cloaca.

Seventh Week: Temporary umbilical herniation is evident; cloaca is divided horizontally into rectum and urogenital sinus; circular and longitudinal musculature differentiates; nerve fibers appear; rectal orifice reaches ectodermal part of cloaca.

Eighth Week: Intestines coil in cord; sublingual gland appears; intestinal villi appear; anal membrane ruptures.

Third Month: Midgut retracts (tenth week); six primary loops form; celom of cord is obliterated; glands of Lieberkühn appear; duodenum becomes fixed by ligament of Treitz, and retroduodenal and duodenal hepatic ligaments; musculature is completed; Auerbach's plexus is completed.

Fourth Month to Birth: Superficial esophageal glands begin to develop (fourth month); meconium accumulates (fourth month); cecum begins revolution and descent into pelvis (fifth month); secondary adhesions develop (fifth month); deep esophageal glands appear; cecum and colon begin to fill (fifth month); lymph nodes and Peyer's patches are indicated (fifth month); haustra are distinct (seventh month); plicae circulares are present (eighth month).

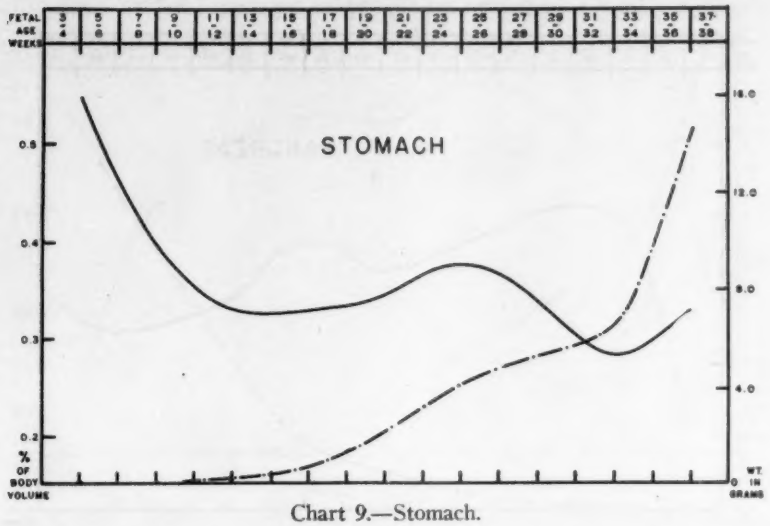

Chart 9.—Stomach.

Fifth Week: Spindle-shaped enlargement of foregut appears; descent into abdomen begins; curvatures begin to appear; fundal bulge is present.

Sixth Week: Rotation to right takes place.

Seventh Week: Pylorus differentiates; mucosal pits appear; circular musculature is present; descent is completed.

Third Month to Birth: Gastric glands begin to differentiate from mucosal pits (fourth month); longitudinal musculature appears (fourth month).

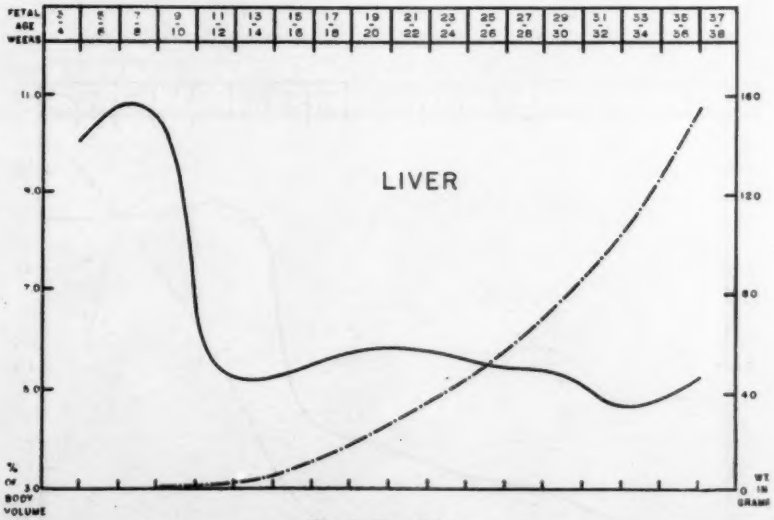

Chart 10.—Liver.

Fourth Week: Anlage appears as median ventral sacculation of foregut into ventral mesentery.

Fifth Week: Cellular cords proliferate; hemopoiesis is evident.

Sixth Week: Solid gallbladder and cystic duct differentiate; lumen appears in common duct; bile capillaries are recognizable; portal venous channel forms from vitelline vein.

Seventh Week: Hepatic artery forms; cystic duct is patent.

Eighth Week: Liver is large, four lobed and symmetric; sympathetic and vagal innervation is evident; interlobular ducts spread.

Ninth Week: Lobulation of portal group is evident; lymphatics are demonstrable.

Tenth Week: Left dorsal lobe begins to atrophy; bile capillaries are abundant.

Twelfth Week to Birth: Gallbladder wall differentiates (twelfth week); bile secretion begins; glands in the neck of the gallbladder differentiate (fourth month).

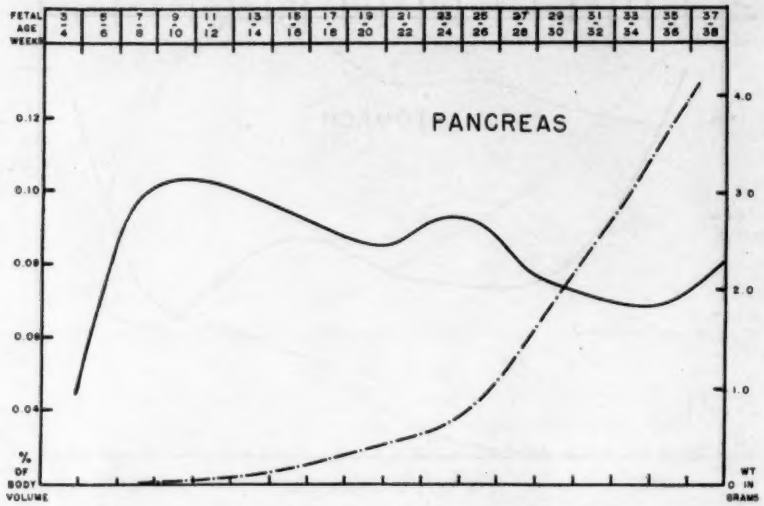

Chart 11.—Pancreas.

Fifth Week: Dorsal and ventral outpocketings form in endodermal lining of duodenum.

Sixth Week: Dorsal part grows more rapidly; ventral duct is carried away from duodenum on common duct.

Eighth Week: Dorsal and ventral anlages interlock; ducts join.

Tenth Week: Alveoli begin to develop.

Eleventh Week: Sympathetic innervation is demonstrable; lymph channels are present; islands begin to appear.

Twelfth Week: Mucous glands are present; ducts bud into islands and acini.

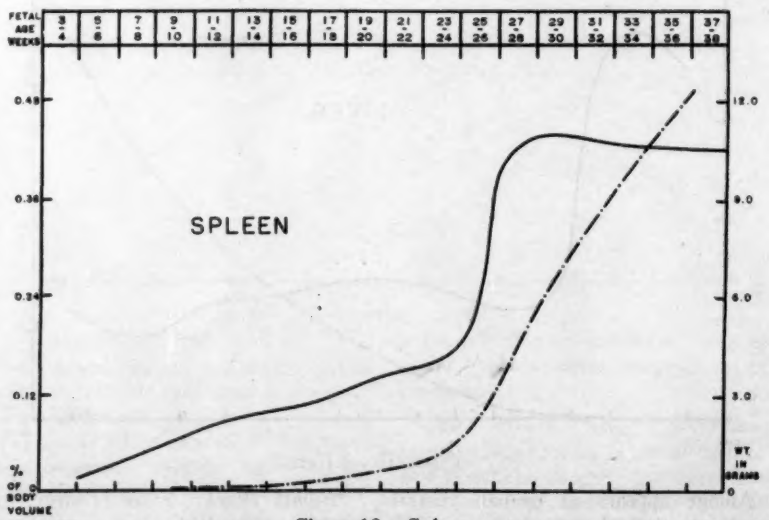

Chart 12.—Spleen.

Sixth Week: Mesenchyme in dorsal mesogastrium proliferates and becomes vascularized.

Third Month: Blood spaces form; surface is nodular and incised; reticulum and corpuscles differentiate.

Fourth Month: Primitive ellipsoids are present; hemopoiesis appears.

Fifth Month: Definite sinuses develop; erythropoiesis is dominant; blood-forming activity reaches maximum.

Sixth Month: Hemopoiesis is ceasing; nodular lymphoid infiltration occurs.

Seventh Month to Birth: Splenic corpuscles are typical (seventh month); spleen acquires typical structure (seventh month).

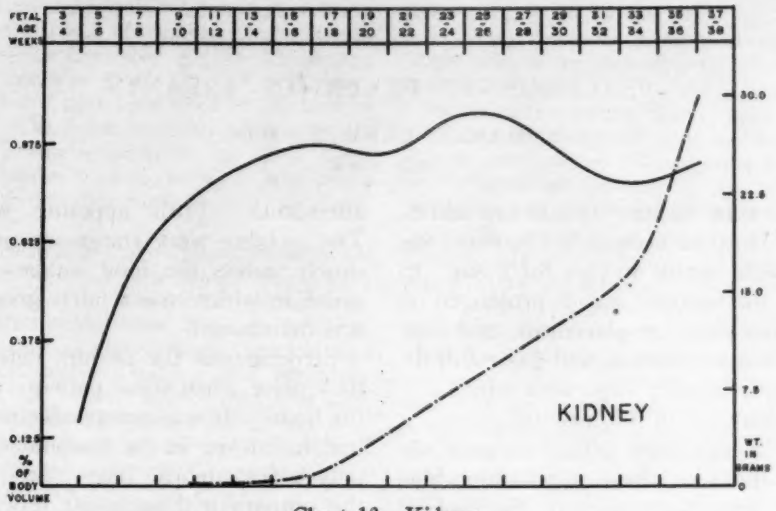

Chart 13.—Kidney.

Fourth Week: Pronephric tubules develop from nephrotome; pronephric duct grows caudad.

Fifth Week: Pronephric duct reaches cloaca as solid cord; pronephros degenerates; mesonephric tubules start to develop from nephrogenic cord; ureteric sac evaginates from mesonephric (pronephric) duct to form ureter and pelvis.

Sixth Week: Primordia of metanephros appear; mesonephric duct is patent; mesonephros reaches maximum; ureteric bud reaches second lumbar level; calyces are forming.

Seventh Week: Mesonephros degenerates; metanephric collecting tubules branch; nephrogenic tissues condense on tubules; earliest secretory tubules form; ascent of metanephros begins; ureter and wolffian duct separate.

Third Month to Birth: Glomeruli appear (tenth week); mesonephric and testicular ducts unite (tenth week); metanephros reaches adrenals (third month); lobulated kidney attains typical shape and structure (fourth month); renal units continue to form (fifth month to after birth).

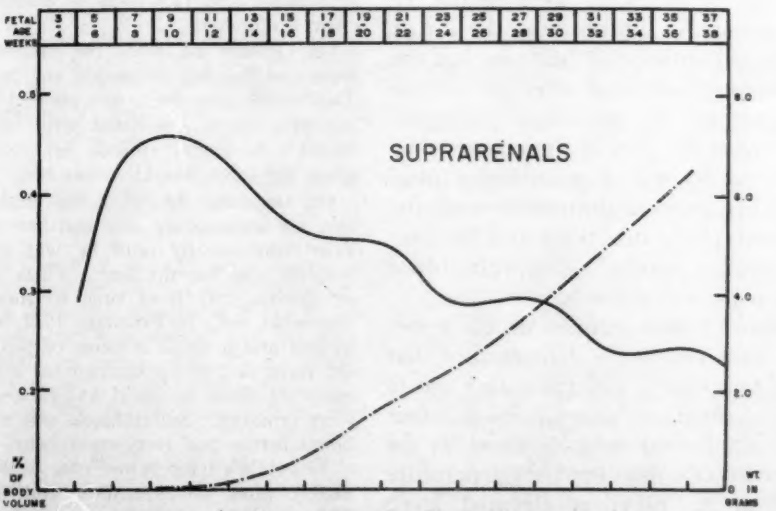

Chart 14.—Adrenal gland.

Fourth Week: Earliest trace of the first part of the adrenal gland (cortex) appears as proliferating peritoneal mesothelium at head of the mesonephros.

Fifth Week: Second part of adrenal gland, sympathicochromaffin tissue from celiac plexus, appears adjacent to cortical primordia to form medulla.

Sixth Week: Vascularization occurs; capsule forms; medullary processes of the sympathicochromaffin cells invade cortex.

Seventh Week: Cell bodies of chromaphil tissues begin to migrate along central vein toward medulla.

Third Month: Cap shape is attained; adult relationship with metanephros is established; adrenal gland is larger than metanephros; gonad and adrenal gland are in contact; mature medullary cells are present (twelfth week); epinephrine is detectable.

Fourth Month to Birth: Involution of fetal cortex (androgenic zone) begins (between fourth and seventh month); migration of sympathicochromaffin cells into medulla continues; true cortex of three layers is apparent after involution of fetal cortex.

Harvard Medical School.

PSYCHOGENIC FEVER IN INFANTS

HARRY BAKWIN, M.D.
NEW YORK

From time to time healthy infants are admitted to Bellevue Hospital because the mothers are ill or are otherwise unable to care for them. In many instances the hospital stay is prolonged on account of technicalities in placement, and during this period cross infections and gastrointestinal upsets not infrequently supervene which further lengthen residence in the hospital.

This report is concerned with 5 infants, observed during the past three years, in whom fever developed after they were in the hospital and persisted for several months. The interval between admission to the hospital and appearance of persistent fever varied from seven to eighteen weeks. Usually the temperature was between 38.3 C. (101 F.) and 39.4 C. (103 F.), but in 1 instance it rose to 41.7 C. (107 F.). No definite cause for the fever could be found. In some instances the pharynx was reddened or an eardrum inflamed, but these conditions were not striking nor were they regularly present or persistent.

Repeated cultures of blood were sterile or showed contaminants. Cultures from the throat occasionally showed pathogenic bacteria, but the temperature remained elevated after the organisms had disappeared; though these pathogens may have accounted for part of the course, they obviously could not be held responsible for all of it. In several instances agglutination tests for typhoid and paratyphoid infections and for brucellosis gave negative results. The white blood cells were not regularly altered.

Administration of sulfonamide drugs sometimes resulted in a fall in the temperature, but this effect was temporary, and continued use of the drugs was without influence. In 1 infant adenectomy was followed by a decrease in the amount of fever for two days but the temperature then reverted to its previous elevated level. Keeping the infants outdoors had no influence on the course of the fever.

The infants did not appear acutely ill; they presented the clinical picture generally seen after prolonged residence in a hospital. They were pale, apathetic, uninterested in their environment and unresponsive to the friendly advances of the attendants. Their appetites were indifferent. The weights were stationary or increased only slowly unless the food intake was larger than usual, in which case a fairly good gain in weight was maintained.

Striking was the prompt defervescence which took place when these patients were returned to the home. It was remarkable to see infants who had had fever in the hospital for months, with only a few afebrile days interspersed, return to the outpatient department repeatedly with normal temperatures.

From the Department of Pediatrics, New York University, and the Children's Medical Service of Bellevue Hospital.

REPORT OF CASES

CASE 1 (Chart 1).—R. K., a Negro boy, was born Sept. 10, 1940 and was transferred from the obstetric to the pediatric ward to await placement in a boarding home because the mother had tuberculosis.

The weight at birth was 5 pounds, 8 ounces (2.5 Kg.). The delivery and early neonatal course were uneventful. When the infant was 18 days old slight cyanosis and twitchings of the extremities were observed. There was no paralysis, irregular respiration or convulsions. The serum contained 8.3 mg. of calcium, 4.5 mg. of phosphorus and 11.5 units of phosphatase per hundred cubic centimeters.

On October 28, when the patient was 7 weeks old, fever and diarrhea developed and lasted for a few days. Two weeks later there was another febrile episode lasting three days, associated with slight redness of the throat. A similar episode occurred two weeks later, when the baby was 11 weeks old.

On December 14, when the infant was 14 weeks of age, his temperature rose and henceforth remained elevated continuously until he was discharged from the hospital, four months later. There were several attacks of rhinitis, and from time to time the pharynx was somewhat red. In February 1941 both ear drums were incised and a small amount of pus was obtained from the right ear, which drained for a few days. On February 29, when the child was 23 weeks old, his adenoids were removed. Sulfathiazole was given for twenty-four hours before and forty-eight hours after the operation.

The child's temperature rose to 40 C. (104 F.) immediately after the operation and then fell to 37.8 to 38.3 C. (100 to 101 F.), where it remained for about two weeks, after which it rose again to about 38.9 C. (102 F.). On April 5 (age, 29 weeks), the day of discharge, the patient's maximum temperature was 38.3 C. (101 F.).

Sulfathiazole was given when the child was 19 weeks old (0.5 Gm. daily for nine days) and again four weeks later (1 Gm. daily for three days) without effect.

The tuberculin test, with amounts up to 1 mg. of tuberculin, gave negative results on two occasions, and a tuberculin patch test made a few days before the infant was discharged from the hospital gave a negative reaction.

The leukocyte count generally fluctuated between 10,000 and 15,000 cells per cubic millimeter of blood throughout the patient's stay in the hospital, the highest count being 22,000 on December 8 (age, 13 weeks), when the temperature was 40 C. (104 F.). Polymorphonuclear cells at this time constituted 50 per cent of the total number. The urine, regularly examined, was always normal. Roentgenograms of the chest taken two and one-half weeks, thirteen weeks, sixteen weeks and twenty-eight weeks after birth showed no abnormalities.

The child received mixtures of evaporated cow's milk and sucrose. Cod liver oil and orange juice were given when he was 2 weeks old. Later ascorbic acid and thiamine hydrochloride were given in addition. The feeding of cereal was started when the child was about 10 weeks of age, and banana and vegetables were added about six weeks later. Iron was also given from time to time. The gain in weight was slow at first but after about twelve weeks was fairly steady with an intake amounting to between 50 and 60 calories per pound of body weight.

Throughout the time that he was in the hospital the infant had spasticity of the lower extremities, for which quinine was given without effect.

hospital. The baby's Wassermann and Kahn reactions were positive on several occasions until she was 7 weeks old; thereafter blood tests showed no syphilis. There was never any clinical or roentgenologic evidence of syphilis.

Intermittent vomiting began when the child was 2 weeks old and continued until she was 5 weeks of age. It was never severe. There were two to four stools daily throughout the hospital stay. The frequency of defecation was not related to the fever.

The diet consisted of evaporated milk and sucrose. This mixture was thickened with cereal when the infant was 3 weeks old because she was vomiting. Viosterol in oil (10 drops daily), ascorbic acid (50 mg.) and thiamine hydrochloride (1 mg.) were added to the diet when the child was 5 weeks old and iron and banana one week later. The milk was acidified with lactic acid from the time the patient was 14 weeks old. Gain in the weight was slow and irregular throughout the time that she was in the hospital.

The erythrocyte count, which had been 3,900,000 cells per cubic millimeter of blood during the third week of life, fell gradually, and when the child was 16 weeks old it was 2,700,000, with a hemoglobin content of 8.4 Gm. per hundred cubic centimeters. The

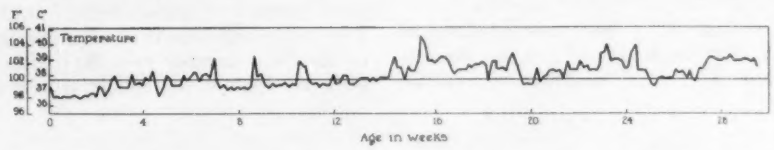

Chart 1 (case 1).—The patient's temperature rose during his fifteenth week in the hospital, and the fever persisted until discharge fourteen weeks later.

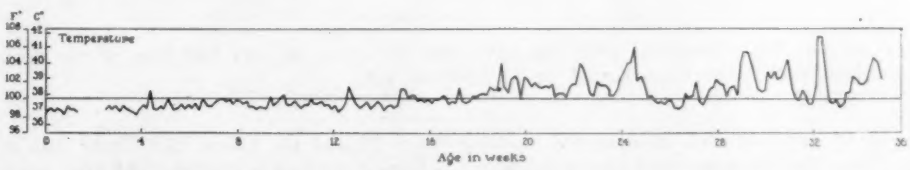

Chart 2 (case 2).—After the child had been in the hospital eighteen weeks her temperature rose, and it remained almost continuously elevated until she was discharged, seventeen weeks later.

When the child was seen four days after discharge from the hospital, he had gained 7 ounces (0.2 Kg.), and his temperature was 38.6 C. (101.4 F.). Three weeks later the temperature was normal and the child had gained more than 17 ounces (0.5 Kg.). Seven weeks later (age, 9 months), the temperature was 37.9 C. (100.2 F.) and the gain in weight 3 pounds and 2 ounces (1.5 Kg.).

When he was 1 year old the patient was readmitted to the hospital with an infection of the respiratory tract and a temperature of 40.6 C. (105 F.). His weight was within the normal range for his age. He had been well since discharge from the hospital except for a spastic paraplegia. An encephalogram showed symmetric areas of atrophy in the midparietal region.

Case 2 (Chart 2).—M. K., a girl, was born by a normal delivery June 4, 1940, after a normal gestation. Her weight at birth was 5 pounds and 10 ounces (2.6 Kg.). The infant was discharged from the obstetric ward on the tenth day, but frequent stools developed shortly afterward and she was readmitted to the infant's ward, at 18 days of age, where the diarrhea subsided quickly. Because the mother was syphilitic, unmarried and an institutional inmate the infant was kept in the

child was pale and apathetic and appeared unhappy. A number of small furuncles appeared while the infant was between 15 and 17 weeks of age, some of which were incised.

During the first eighteen weeks that the infant was in the hospital her temperature was normal except for an occasional elevation. It then rose gradually, reaching 40 C. (104 F.) when she was 19 weeks old. Examination disclosed no abnormalities except for a reddened pharynx. There were 9,000 white cells per cubic millimeter of blood, and cultures of urine and of exudate from the throat were sterile. The fever persisted, and after nine days sulfathiazole was given for sixty hours without any effect.

When the child was 22 weeks old, therapy with neoarsphenamine was begun. Seven doses of 75 mg. each were given over a period of about four weeks.

Two weeks later the child's temperature rose to 41.1 C. (106 F.), where it remained for forty-eight hours. Examination revealed only a slightly reddened pharynx. A culture of the blood was sterile; there were 9,000 cells per cubic millimeter of blood, and the urine was normal. After this episode the temperature fell to normal and remained there for about two weeks. It

then began to climb again, reaching 40.6 C. (105 F.) when the infant was 29 weeks old. Again no adequate explanation for the fever was found.

A week later the child had a stomatitis. Sulfathiazole was given for five days (0.5 Gm. daily). The temperature fell to normal after two days, but at the age of 32 weeks the child had another febrile episode, with a temperature of about 41.7 C. (107 F.) for forty-eight hours. She seemed surprisingly well on the first day despite the fever but wilted appreciably later. The pharynx was fiery red and pharyngeal exudate showed hemolytic streptococci on culture. Cultures of blood and urine were sterile. There were 7,500 white cells per cubic millimeter of blood. The temperature fell to normal forty-eight hours after sulfathiazole was given, remained there for four days and then rose again. During the two days before she was discharged from the hospital the child had a temperature of 40 C. (104 F.). It was 38.9 C. (102 F.) on February 5, the day of discharge.

The child was seen six days after discharge and frequently during the remainder of the year 1941. Her temperature on each occasion was normal. She gained rapidly and at the age of 18 months weighed 23 pounds and 3 ounces (10.5 Kg.). When last heard from she was 26 months old and well.

CASE 3 (chart 3).—R. B., a boy, was admitted to the hospital May 12, 1940, at the age of 5 weeks, because of disease of the right eye. The condition began when the infant was 12 days old with redness and swelling of the lids. There was some purulent discharge, which failed to show pathogenic organisms on repeated examinations. The entire cornea was ulcerated, and scarring resulted despite intensive therapy.

The infant was born April 9, 1940, weighing 6 pounds and 10 ounces (3 Kg.). The delivery and postnatal course were normal except for the infection of the eye. The feeding consisted of cow's milk and dextrimaltose, to which orange juice (60 cc. daily) and cod liver oil (8 cc.) were added when the infant was 1 month old, cereal and banana at 3 months and vegetable at 4 months. Riboflavin and vitamin B complex were also given because of the ophthalmic lesion.

During the first three weeks in the hospital the child had a normal temperature. In the fourth and fifth weeks in the hospital he had abrupt rises in temperature of brief duration, presumably owing to absorption of atropine which he was receiving as eye drops. From the end of the third week in the hospital until his discharge eight months later his temperature was almost continuously elevated, usually between 38.3 C. (101 F.) and 38.9 C. (102 F.), sometimes up to 39.7 C. (103.5 F.). The longest afebrile period was seventeen days (age 21 to 23 weeks).

Repeated examinations failed to reveal any cause for the fever except an acute nasopharyngitis and catarrhal otitis media when the patient was 15 weeks old and a mild pharyngitis when he was 22 weeks of age. When the patient was 19 weeks old culture of material from the throat showed occasional pneumococci, which could not be typed.

Because the child at 34 weeks of age had palpable cervical, axillary and inguinal lymph nodes and a broad upper mediastinal shadow, the presence of a lymphosarcoma was suspected, and roentgen radiation was given to the mediastinum. The sternal marrow was normal. A pea-sized node was removed from the supraclavicular region and was reported as showing giant follicular lymphadenopathy. After transfer of the child to the surgical ward for removal of a specimen for biopsy, his temperature, which had been continuously elevated for over two months, fell to normal and remained there for seven days. It rose again on the day before the child returned to the medical ward.

During the entire time in the hospital the baby was apathetic and uninterested in his environment but did not appear acutely ill. Food was taken well, and there was no vomiting. There were two to four stools a day without episodes of diarrhea. He gained weight slowly and irregularly and was more than 4½ pounds below average on discharge. In general, the child gained less rapidly when his temperature was high than when it was only slightly elevated. The eye healed with clouding and scarring of the right cornea and loss of vision.

The leukocyte count did not fluctuate significantly from normal (highest count, 14,250; lowest, 6,450). The polymorphonuclear cells constituted 80 per cent of the total number two days after admission; thereafter the highest percentage of polymorphonuclear cells was 72 and the lowest 28. There was a mild anemia (lowest level of hemoglobin, 8.8 Gm. per hundred cubic centimeters at the age of 4½ months). Regular examinations showed the urine to be normal.

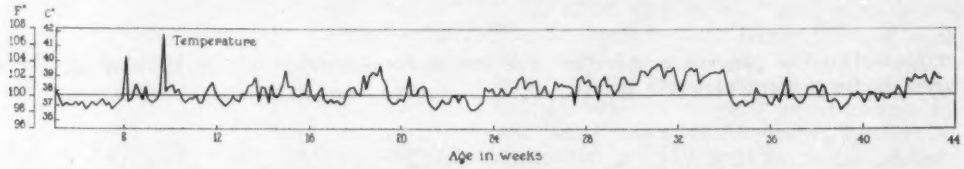

Chart 3 (case 3).—Fever appeared when the baby was 14 weeks old and had been in the hospital for nine weeks. It persisted until he was discharged, at 43 weeks of age.

Repeated cultures of material from the throat were sterile except one taken when the infant was 18 weeks old, which showed occasional pneumococci. Blood agglutinations for typhoid and paratyphoid and for brucellosis were negative when the child was 19 weeks and 22 weeks of age, and the heterophile antibody test gave agglutination within the normal range of dilutions when he was 19 weeks old. Cultures of blood when the infant was 18, 28 and 31 weeks old were sterile, and a culture of stools when he was 18 weeks showed no pathogenic organisms.

At 19 and again at 37 weeks the child reacted negatively to tuberculin in amounts up to 1 mg. Repeated roentgenograms of the chest showed no changes except for a mediastinal shadow which was somewhat broad. Roentgenograms of the long bones when the patient was 14, 18 and 32 weeks old were normal.

Sulfathiazole was given to the child for the ocular infection a few days after he was admitted to the hospital, before pyrexia developed. Sulfanilamide was given for four days during the twenty-first week after birth without effect. Subsequent administration of sulfathiazole was followed by a drop in fever, but it was tried again for six days when the infant was 25 weeks and for four days when he was 27 weeks old without effect.

The child was discharged from the hospital on Feb. 2, 1941, at the age of 10 months, with a temperature of 38.5 C. (101.3 F.). The daily maximum temperature for ten days before discharge had been 38.9 C. (102 F.). His weight at that time was 15 pounds, 8 ounces (7.0 Kg.). The infant was somewhat retarded in mental and motor development. He was unusually quiet, and he was unable to support his head properly or to sit alone.

He was next seen on April 24, 1941, eleven weeks after he was discharged from the hospital. He was 54 weeks old. He had gained 6 pounds (2.7 Kg.) and while at home he had not been acutely ill. His temperature was 38.1 C. (100.6 F.). He was again seen when he was 2 years old. In the interim he had been well without any febrile episode. His weight at this time was 32 pounds, 5 ounces (14.7 Kg.) and his temperature 37.9 (100.2 F.). He was mentally retarded. The lymph nodes were not enlarged.

CASE 4 (chart 4).—W. K., a boy, was born on April 4, 1940, after thirty-seven weeks of gestation. His weight at birth was 4 pounds, 6 ounces (2.0 Kg.). He remained in the special unit for prematurely born infants for twelve weeks and was discharged June 26, 1940, weighing 6 pounds, 3 ounces (2.8 Kg.). After repeated examinations. Cultures of material from the stools and from the throat contained no pathogenic organisms. White blood cell counts were normal throughout. Tuberculin tests when the child was 10 weeks and 24 weeks old gave negative reactions with amounts up to 1 mg. Roentgenograms of the chest taken when the infant was 13, 20 and 23 weeks old were normal. At 23 weeks of age, he was given sulfathiazole (1.5 Gm. daily) for three days. His temperature fell to normal and remained there for six days but then rose again.

During the first six weeks of life the infant received breast milk; thereafter he was given mixtures of evaporated cow's milk and dextrimaltose. Vitamin D, iron and ascorbic acid supplements were added to this diet early and banana, cereal and vegetables at a later time. After the first few weeks of life, the infant received 55 to 65 calories per pound of body weight. His appetite was good throughout. There was no vomiting. There were two to three stools a day, with episodes in which frequent stools occurred. Gain in weight during the time the child was in the hospital was slow and irregular, the net gain during the first six months amounting to 4 pounds, 3 ounces (1.9 Kg.).

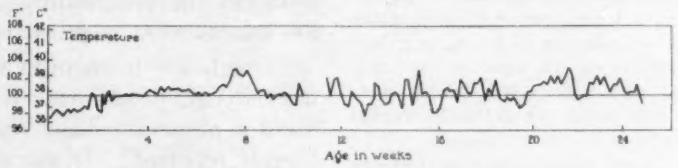

Chart 4 (case 4).—Fever developed in a prematurely born infant after eleven weeks in the hospital and persisted until the patient was discharged, thirteen weeks later.

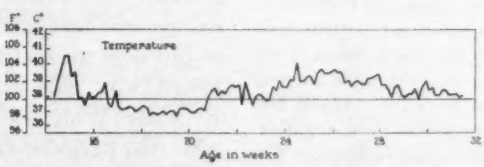

Chart 5 (case 5).—Diagnosis, congenital syphilis. Fever appeared when the child was 21 weeks of age, seven weeks after he was admitted to the hospital, and persisted until he was discharged, ten weeks later.

the first three weeks that he was in the hospital his temperature rose, going to 38.3 C. (101 F.) almost daily. Between June 3 and June 13 the temperature level was about 38.9 C. (102 F.). For a week before he was discharged his temperature was normal except on the last day, when it was over 38.3 C. (101 F.). No cause for the fever could be found. During his stay in the hospital he made a fair gain in weight. Occasionally there were frequent stools.

The child was readmitted to the hospital on July 2, 1940, at 13 weeks of age, one week after discharge. The mother had died of tuberculosis six weeks after the baby's birth and the father was in a sanatorium for tuberculosis. The grandmother, who had volunteered to take the baby, was unable to carry on.

On readmission the child weighed 6 pounds (2.7Kg.), and his temperature was 37.9 C. (100.2 F.). The infant remained in the hospital for three months, and during this time his temperature rose almost daily. The longest afebrile period was seven days before discharge. The usual temperature range was between 38.3 C. (101 F.) and 38.9 C. (102 F.).

No cause for the fever could be found except for a slightly reddened pharynx. Occasionally there were loose and frequent stools. The urine was normal on

The child was discharged to the Speedwell Boarding-Out Unit Oct. 1, 1940, at 26 weeks of age, weighing 8 pounds, 6 ounces (3.9 Kg.). He was next seen by me seven weeks later. His temperature was normal, and he had almost doubled his weight, a gain of 7 pounds, 5 ounces (3.3 Kg.). When last seen he was 13 months old, weighed 26½ pounds (12.1 Kg.) and was well.

CASE 5 (chart 5).—K. R., a Negro boy, was admitted to the hospital on July 19, 1941 because of mild vomiting and diarrhea. He was 14 weeks old and weighed 8 pounds, 6 ounces (3.8 Kg.). He was the second child of parents both of whom had syphilis. The prenatal course, delivery and neonatal period were normal. The weight at birth was 6 pounds (2.7 Kg.).

The child's temperature on admission was 37.9 C. (100.2 F.). During the next three days it rose gradually to 40.6 C. (105 F.), and it then remained elevated for six days. Examination at this time showed no cause for the fever. Cultures of blood, urine and stools were sterile. Cultures of material from the nose and throat contained no pathogenic organisms. A roentgenogram and fluoroscopic examination of the chest showed no abnormality. There were 14,400 leukocytes per hundred cubic centimeters of blood, with 44 per cent of them

polymorphonuclear. On the fourth day of his illness the child was given sulfathiazole (0.75 Gm. daily). His temperature fell to normal in forty-eight hours but rose again after three days and remained elevated for six days.

A Wassermann test of the blood gave a 4 plus reaction. There were no clinical manifestations of syphilis. Roentgenograms of the long bones were normal. On August 6 (age 17 weeks) intensive antisyphilitic treatment was started. A total of 38 mg. of mapharsen was given over a period of six days without unfavorable reaction.

The infant was free from fever for about five weeks. On September 3, when he was 21 weeks of age, his temperature rose, and thereafter it remained elevated until he was discharged ten weeks later.

At the beginning of the febrile period there was a slight cough and nasal discharge. The pharynx was red, and both ear drums were injected. Eight days later the left ear drum ruptured and four days later the right drum. Both drums were incised. Cultures of material from the ears showed staphylococci and Bacillus pyocyaneus. The left ear healed promptly, but the right ear continued to drain profusely for almost three weeks. Starting on September 29 (age of patient 24 weeks) sulfathiazole (1.2 Gm. per day) was given for three days and later sulfadiazine (1.2 Gm. per day) for two days without influencing the fever or the aural discharge. Sulfadiazine and later sulfanilamide were also given in October (age of patient 26 to 28 weeks) without favorable effect.

The temperature remained elevated during October (about 38.9 C. (102 F.), but no reason for the fever could be found. Cultures of the blood and urine and of material from the nose and throat were not remarkable except for one throat culture, made on October 9, in which 75 per cent of the colonies were hemolytic streptococci. Roentgenograms of the chest taken when the child was 14, 21, 22 and 24 weeks old were normal, and the reactions to agglutination tests for typhoid and paratyphoid infections and for brucellosis were negative. The urine was normal on repeated examinations. The number of white cells in the blood was within the normal range at all times. The reaction to the Mantoux test was negative.

For the first ten days in the hospital the infant received protein milk. Thereafter he was given evaporated cow's milk and sucrose with ascorbic acid and thiamine hydrochloride supplements. Orange juice and cereal were added when he was 20 weeks and vegetables and fruit when he was 28 weeks old. The gain in weight on an intake between 50 and 60 calories per pound was slow, and the child never made up the weight deficit from which he suffered on admission. The appetite was good; there were usually two to three stools a day, and there was no vomiting.

The infant was discharged from the hospital on Nov. 15, 1941, with a temperature of 38 C. (100.4 F.). He was 7 months old and weighed 12 pounds, 13 ounces (5.8 Kg.). Reactions to both the Wassermann and the Kahn test were positive.

The child was first seen in the outpatient department two weeks after discharge from the hospital. He had gained 2 pounds (0.9 Kg.) and his temperature was normal. He was again seen two weeks later and a third time three weeks thereafter. In the first seven weeks after leaving the hospital he gained over 4 pounds (1.9 Kg.). On a second admission to the hospital for sixteen days in January 1942 (age 9 months) for another course of antisyphilitic therapy, the child had a normal temperature except on two occasions, on which it rose to 37.8 C. (100 F.). He was last seen on March 9, 1943, at 23 months of age. He weighed 28 pounds (12.7 Kg.) and was receiving antisyphilitic treatment. Aside from the infection with syphilis as shown by a positive reaction to the Wassermann test, he was well.

COMMENT

Infants who remain in hospitals for a considerable length of time frequently acquire infections, usually of the nose and throat, and these infections tend to persist for a longer time than when the infants are cared for in the home. In many instances febrile episodes take place for which no cause can be readily found. Some of these febrile reactions are attributable to obscure infections, of the genitourinary tract for example, but often no specific cause can be demonstrated even after careful, prolonged study. Five such infants with fever which persisted for from three to eight months are described in this report. In all instances the temperature fell to normal when the infants were returned to the home.

Though the mechanism has not been clearly worked out, psychogenic fever has been recognized in adults for many years and has been frequently reported.[1] It was mentioned as a manifestation of "hysteria" by Osler[2] in 1894. In 1914 Friedemann and Kohnstamm[3] described patients in whom fever was associated with excitement and emotional tension in the absence of physical overactivity. Somewhat later Eichelberg[4] was able to induce fever by hypnosis. Recently Wolf and Wolff[5] described a patient who had periodic sick headaches for many years and recurrent bouts of fever (temperatures up to 40 C. (104 F.) over a period of thirteen years. Despite intensive study a cause for the fever was never discovered. Numerous therapeutic measures were ineffective. The bouts of fever stopped after the patient was given an opportunity to ventilate his personality conflicts, of which he had many, but the attacks reappeared when he returned to a setting of unusual tension and anxiety. The authors believe the fevers were due to a "temporary derangement in the

1. Dunbar, H. F.: Emotions and Bodily Changes, ed. 2, New York, Columbia University Press, 1938, pp. 197-205.

2. Osler, W.: Principles and Practice of Medicine, New York, D. Appleton and Company, 1894, p. 975.

3. Friedemann, M., and Kohnstamm, O.: Zur Pathogenese und Psychotherapie bei Basedowscher Krankheit, Ztschr. f. d. ges. Neurol. u. Psychiat. **23**:357, 1914.

4. Eichelberg: Durch Hypnose erzeugtes, "Hysterisches Fieber," Deutsche Ztschr. f. Nervenh. **68-69**: 352, 1921.

5. Wolf, S., and Wolff, H. G.: Intermittent Fever of Unknown Origin, Arch. Int. Med. **70**:293 (Aug.) 1942.

thermoregulatory centers of the brain, possibly of a vascular nature, arising in a setting of anxiety and insecurity in a rigid, compulsive person who has had migraine."

Wolf and Wolff [5] classify "neurogenic" fever into four types: (1) factitious fever, extremely high temperatures, generally regarded as incompatible with life, induced by fraudulant methods, (2) habitual low grade fever, (3) isolated rises in body temperature of short duration associated with some experience inducing anxiety or tension and (4) recurrent bouts of high fever which occur over a period of years without interfering with the general health of the patient.

In children, too, elevations of temperature have been ascribed to emotional upsets. Minor elevations in temperature are occasionally observed in young children when they are brought to the physician's office. Pototzky [6] mentioned children in whom fever occurs even before they start to eat foods toward which they have an aversion. He also spoke of "school fever" in children who find the school situation unpleasant. He suggested that psychogenic fever may be present in nervous children whose temperature is taken daily by an overanxious mother, and this view has also been expressed by Horder.[7] In these children discontinuance of daily taking of temperature results in a disappearance of the fever as indicated by occasional control measurement later.

The profound alterations in function and behavior in infants which result from prolonged residence in hospitals has been recognized for a long time.[8] That these changes are due principally to emotional deprivation seems highly probable. There are many reasons for believing this,[9] but the best proof is the prompt change in physical status and in behavior when infants are transferred from the impersonal environment of the hospital to the personalized atmosphere of the home. It is my belief that the prolonged fever of infants in hospitals is also related to emotional deprivation, since it, too, promptly disappears when the infants are returned to the home. One would hardly expect that fever of infectious origin, after lasting for several months, would disappear so quickly and so regularly solely as a result of transferral of the patient from hospital to home. It is possible that, because of the relative inactivity of the baby in the hospital, there might be pooling of infected material in the nasopharynx; but there is no evidence, clinical or otherwise, to substantiate such a hypothesis.

It is conceivable that the fever of infants in hospitals is actually due to infection and that the psychic disturbances which accompany residence in an institution lead to an altered reactivity and a prolongation of the course. Each of the infants in this series, at one time or another, showed clinical evidence of infection, usually of the nose, throat and ears. But this mechanism still places on psychic factors the principal role in explaining the persistence of the fever.

SUMMARY

In 5 infants fever developed after they had resided in a hospital for some time and lasted from three to eight months. In all the infants the temperature fell to normal within a few days after they were returned to the home.

It is suggested that either the prolonged fever was primarily psychogenic or psychic factors led to a continuation of fever which was due to an ordinary infection of the upper respiratory tract.

132 East Seventy-first Street.

6. Pototzky, C., in Schwarz, O.: Psychogenes und Psychotherapie körperlicher Symptome, Vienna, Julius Springer, 1925, p. 409.

7. Horder, T.: Some Cases of Pyrexia Without Physical Signs, Canad. M. A. J. **16**:130, 1926.

8. Chapin, H. D.: Are Institutions for Infants Necessary? J. A. M. A. **64**:1 (Jan. 2) 1915.

9. Bakwin, H.: Loneliness in Infants, Am. J. Dis. Child. **63**:30 (Jan.) 1942.

RHEUMATIC INFECTIONS IN CINCINNATI HOSPITALS

STUDY OF 3,475 ADMISSIONS FROM 1930 TO 1940; COMPARISON WITH INCIDENCE IN PHILADELPHIA HOSPITALS FROM 1930 TO 1934

ARNOLD G. WEDUM, PH.D., M.D., AND BERNICE G. WEDUM, M.D.
CINCINNATI

The syndrome of rheumatic fever, with its major manifestations of polyarthritis, heart disease and chorea, is becoming increasingly important from the standpoint of public health.[1] Yet with the causation, diagnosis and treatment still poorly defined, compared for example with those of a disease such as syphilis, a wholly satisfactory method of coping with this infection remains to be found.

One approach to a better understanding of the nature of rheumatic infections has been provided by an analysis of hospital admissions for this disease. The most comprehensive recent reports of this sort have dealt with Philadelphia,[2] and New Haven,[3] where the records of all hospitals were examined. Studies covering an entire city have been infrequent because of the difficulties involved in reviewing the records of a large number of hospitals. One of the values of such a study is that it provides a basis for estimating the number of beds required for adequate convalescent care of patients with rheumatic heart disease.[4]

The present study was designed to analyze the nature of the conditions of hospitalized patients with rheumatic infections in Cincinnati so that comparison might be made with other communities. It was thought that comparison with Philadelphia might be fruitful because geographically and climatically the two cities are much alike. Both lie on the thirty-ninth parallel of latitude, on rivers away from the seacoast. The mean annual temperature for January is 30 F. in Cincinnati and 33 F. in Philadelphia; the temperatures for July are 75 F. and 76 F. respectively. The mean annual precipitation is 38.5 inches (36.8 cm.) in Cincinnati and 40.3 (41.5 cm.) in Philadelphia. Philadelphia is by far the larger city, with a population of roughly 2,000,000, while that of Cincinnati is only about 500,000. The populations of both have about the same Negro component—10.6 per cent in Cincinnati and 11.3 per cent in Philadelphia (1930). Both are industrial trading cities; both also are university centers.

In addition to the advantage provided by the similarity of the two cities, the study by Hedley[2] on rheumatic heart disease in hospitals in Philadelphia provided excellent data for comparison and a pattern on which our own study was modeled.

PROCEDURE

The records of all admissions to all hospitals in Cincinnati from Jan. 1, 1930 to Dec. 31, 1940 which bore a primary or secondary diagnosis of rheumatic heart disease, rheumatic fever, rheumatic polyarthritis or chorea were examined by the authors. A check was made of the records of each hospital to secure reports of cases filed solely under anatomic or physiologic diagnoses. The following types of hospitals were not included in the survey in either Cincinnati or Philadelphia: military and penal hospitals and hospitals for persons with nervous and mental diseases, tuberculosis and cancer. Outpatient and dispensary cases were omitted.

It should be noted that a distinction has been made between cases and admissions. One case represents the records of one hospital on 1 person and may include 1, 2 or more admissions.

The diagnoses made in each hospital were usually accepted as correct. The basis for the interpretation of murmurs was much the same as that discussed by Paul.[3] Our policy was to exclude doubtful cases. Most of the exclusions were for the older age groups. Before a case was included in this study the entire hospital record was surveyed in detail. Not examined were the records of those cases of subacute bacterial endocarditis in which a diagnosis of rheumatic heart disease was not made. In Philadelphia all records of subacute bacterial endocarditis were examined, and some of these may have been accepted as cases of rheumatic disease in the survey of that city.

From the Department of Bacteriology, University of Cincinnati College of Medicine, the Max Stern Heart Station for Rheumatic Heart Disease, and Children's Hospital.

1. Swift, H. F.: Public Health Aspects of Rheumatic Heart Disease, J. A. M. A. **115**:1509 (Nov. 2) 1940.

2. Hedley, O. F.: Rheumatic Heart Disease in Philadelphia Hospitals, Pub. Health Rep. **55**:1599 (Sept. 6); 1647 (Sept. 13); 1707 (Sept. 20); 1809 (Oct. 4); 1845 (Oct. 11) 1940.

3. Paul, J. R.: Rheumatic Fever in New Haven, Lancaster, Pa., Science Press Printing Company, 1941.

4. Wedum, B. G., and Wedum, A. G.: A Method for Determining the Number of Beds Required for Convalescent Care of Rheumatic Infections, Am. J. Pub. Health **32**:1237 (Nov.) 1942.

RELATION OF ADMISSIONS FOR RHEUMATIC DISEASE TO ALL HOSPITAL ADMISSIONS

During the eleven years from 1930 through 1940 there were 593,032 admissions to the Cincinnati hospitals studied, of which 3,475, or 0.59 per cent, were for rheumatic infections. The comparable figure for Philadelphia was 0.68 per cent.[2] In other words, in Cincinnati 6 admissions of every thousand were of persons with rheumatic infections and in Philadelphia 7 of every thousand.[5]

Examination of table 1 (admissions) and table 2 (cases) shows that according to the chi square test there was no significant difference between the two cities in the amount of uncomplicated rheumatic fever and uncomplicated chorea. But according to the chi square test, there was much more uncomplicated rheumatic heart disease in Cincinnati. Conversely, there was in Cincinnati much less of the complicated forms of the disease, namely, rheumatic heart disease with subacute bacterial endocarditis, rheumatic heart disease with rheumatic fever and rheumatic heart disease with chorea. The apparent difference between the two cities in the incidence of rheumatic heart disease with subacute bacterial endocarditis is partly real and partly a result of differences in the methods of survey.[6]

TABLE 1.—*Number of Admissions for Treatment of Rheumatic Infections and Percentage of Total Hospital Admissions in Ten Hospitals in Cincinnati from Jan. 1, 1930 to Dec. 31, 1940, Compared with Similar Data for Thirty-Six Philadelphia Hospitals During the Years 1930 to 1934, Inclusive*

	Number of Admissions			Percentage of Total Admissions	
	Philadelphia	Cincinnati	χ^2*	Philadelphia	Cincinnati
Rheumatic heart disease with rheumatic fever and subacute bacterial endocarditis	...	9			
Rheumatic heart disease with subacute bacterial endocarditis	223	50	24.7	0.026	0.011
Rheumatic heart disease with rheumatic fever and chorea	30	13	1.0	0.004	0.002
Rheumatic heart disease with rheumatic fever	930	372	43.9	0.109	0.063
Rheumatic heart disease with chorea	332	100	32.4	0.039	0.017
Rheumatic heart disease, uncomplicated	3,354	2,394	43.0	0.394	0.404
Rheumatic fever with chorea but no rheumatic heart disease	11	10	0.9	0.001	0.002
Rheumatic fever, uncomplicated	488	292	0.0	0.057	0.049
Chorea, uncomplicated	433	226	2.8	0.051	0.038
Total rheumatic infections	5,801	3,475	148.7	0.682	0.586
Total admissions	850,423	593,032			

* Calculated from differences between observed and expected frequencies of the various manifestations of rheumatic infection in the two cities. The very large value of χ^2 may be interpreted as adequately disproving the hypothesis that the two cities, in this respect, are random samples of the same population.
For $\chi^2 = 148.7$, $N = 7$, P is a very small number.

TABLE 2.—*Number of Cases of Rheumatic Infections in Ten Hospitals in Cincinnati from Jan. 1, 1930 to Dec. 31, 1940, Compared with Similar Data for Thirty-Six Hospitals in Philadelphia from Jan. 1, 1930 to Dec. 31, 1934*

	Number of Cases		
	Philadelphia	Cincinnati	χ^2*
Rheumatic heart disease with subacute bacterial endocarditis	209	60	12.7 P†
Rheumatic heart disease with rheumatic fever and chorea	30	8	2.3
Rheumatic heart disease with rheumatic fever	808	312	10.9 P
Rheumatic heart disease with chorea	259	52	35.2 P
Rheumatic heart disease, uncomplicated	2,348	1,338	24.5 C
Rheumatic fever with chorea but no rheumatic heart disease	11	7	0.3
Rheumatic fever, uncomplicated	475	247	1.0
Chorea, uncomplicated	387	154	4.0
Total rheumatic infections	4,527	2,178	90.9 P

* χ^2 calculated from differences between observed and expected frequencies of the various manifestations of rheumatic infection in the two cities. For $\chi^2 = 90.9$, $N = 7$, P is a very small number.
† C indicates comparatively more in Cincinnati; P, comparatively more in Philadelphia.

5. Statistically the difference between 0.59 and 0.68 per cent is tremendously significant. χ^2 equals 50.6 with P a very small number.

AGE DISTRIBUTION OF CASES OF RHEUMATIC INFECTION

Rheumatic heart disease, both complicated and uncomplicated, comprised about 81 per cent of all rheumatic infections in both cities, but in Cincinnati hospitals it occurred in fewer young persons and in more old persons (fig. 1). In every age group up to the age of 34 years there was less rheumatic heart disease in Cincinnati than in Philadelphia; in the groups above the age of 34 years there was more.

In Cincinnati one half of the patients with rheumatic heart disease were under the age of 30 years; in Philadelphia, two thirds. In clinics for persons with cardiac disease in New York, 53 per cent of the patients with rheumatic infections were less than 20 years of age when they first came under observation.[7] Actual hospitalization, however, might be expected to occur later

6. See paragraph three under "Procedure."

7. Cohn, A. E., and Lingg, C.: The Natural History of Rheumatic Cardiac Disease: I. Onset and Duration of Disease, J. A. M. A. **121**:1 (Jan. 2) 1943.

in life. In Philadelphia, 48 per cent of the patients with rheumatic infections were under 20 years of age at the time of initial hospitalization; in Cincinnati, 34 per cent. This age distribution is consistent with the lower incidence (tables 1 and 2) in Cincinnati of the more

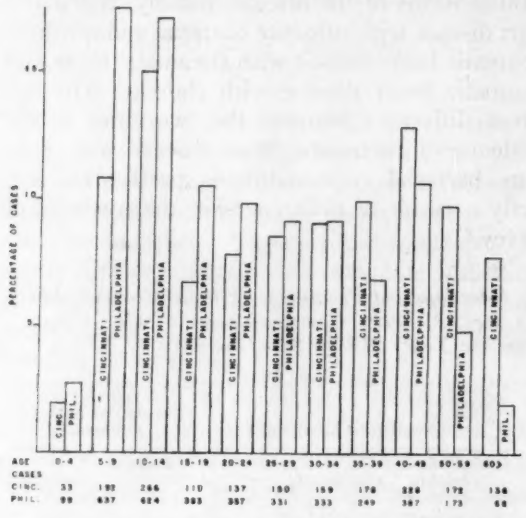

Fig. 1.—Percentage distribution by age periods of patients of 1,764 cases of rheumatic heart disease in ten Cincinnati hospitals from 1930 to 1940, based on age at initial admission during period under study, compared with 3,641 cases in thirty-six Philadelphia hospitals from 1930 to 1934. Four other cases, for which the patients' ages are unknown, occurred in Cincinnati; 13, in Philadelphia.

However, much less chorea complicated by rheumatic heart disease was found in Cincinnati than would be expected. Of 221 cases of chorea in Cincinnati 60, or 27 per cent, were complicated by rheumatic heart disease, compared with 42 per cent in Philadelphia and 46.5 per cent as an average for cases reported in the literature.[2] This is further evidence of a lessened severity of rheumatic infections in Cincinnati.

TABLE 4.—*Annual Incidence* per Hundred Thousand of Population in Each Age Group (Census 1930) of Cases of Rheumatic Infections in Hospitals Among White Persons and Negroes*

	White		Negro	
	Cincinnati	Philadelphia	Cincinnati	Philadelphia
All rheumatic infections †.....	41.7	45.4	62.0	55.6
All rheumatic heart disease				
Age 0 to 24 years.....	35	49	63	61
Age 25 to 34 years.....	34	39	48	41
Age 35 to 44 years.....	36	31	54	23
Age 45 years and over.....	31	17	21	27
All rheumatic fever				
Age 0 to 24 years.....	18	20	41	41
Age 25 to 34 years.....	9	11	22	22
Age 35 to 44 years.....	7	6	20	12
Age 45 years and over.....	2	2	3	6
All chorea				
Age 0 to 14 years.....	19	28	10	13

* Cincinnati, 2,178 patients 1930 to 1940; Philadelphia, 4,538 patients 1930 to 1934.
† The figures 45.4 and 55.6 depend on a racial segregation of patients admitted which could be obtained only as an approximation by calculation from Hedley's tables.[2]

TABLE 3.—*Distribution of Cases of Rheumatic Heart Disease According to the Age and Race of the Patient*

	White					Negro				
	Cincinnati		Philadelphia			Cincinnati		Philadelphia		
Age	Number of Cases	Percentage	Number of Cases	Percentage	χ^2	Number of Cases	Percentage	Number of Cases	Percentage	χ^2
Under 5 years.....	28	1.9	88	2.8	3.5	5	1.9	11	2.3	0.1
5 to 14 years.....	372	24.8	1,093	34.6	31.1	86	32.2	168	34.8	0.3
15 to 24 years.....	207	13.8	635	20.1	22.4	49	18.3	105	21.7	1.0
25 to 34 years.....	254	16.9	559	17.7	0.3	56	21.0	105	21.7	0.3
35 to 44 years.....	250	16.7	419	13.3	14.6	52	19.5	46	9.5	13.0
45 to 59 years.....	258	17.2	304	9.6	48.3	14	5.2	40	8.3	2.2
Over 60 years.....	131	8.7	60	1.9	115.8	5	1.9	8	1.7	0.0
Total.....	1,500*	100.0	3,158†	100.0	236.0	267	100.0	483‡	100.0	16.9

* 3 others, age unknown.
† 12 others, age unknown.
‡1 other, age unknown.

For N = 6, χ^2 = 236, P is a very small number.
For N = 6, χ^2 = 16.9, P is about 0.01.

acute manifestations of the rheumatic syndrome, which occur more frequently in youth.

When age distribution is considered by race (table 3) and racial distribution by annual incidence per hundred thousand of population (table 4), it is clear that only white children in Cincinnati have a low incidence of infection. Negroes at all ages have an incidence approximately equal to, or greater than, that for the general population in Philadelphia.

In both cities 89 per cent of all cases of chorea occurred between the ages of 5 and 14 years.

SEX DISTRIBUTION OF CASES OF RHEUMATIC INFECTION

Rheumatic infections in general and rheumatic heart disease in particular are regarded as more prevalent among girls and women than among men and boys.[8] This concept was corrobo-

8. (*a*) Hedley.[2] (*b*) Stroud, W. D., and Twaddle, P. H.: Fifteen Years' Observation of Children with Rheumatic Heart Disease, J. A. M. A. **114**:629 (Feb. 24) 1940. (*c*) Swift, H. F.: Rheumatic Fever, in Cecil, R. L.: Textbook of Medicine, ed. 5, Philadelphia, W. B. Saunders Company, 1940.

rated by the present study to the extent that 56 per cent of all rheumatic infections, 57 per cent of all rheumatic heart disease and 59 per cent of the chorea occurred in girls and women (table 5). It is difficult to determine whether these differences are statistically significant, because there is a general tendency for more boys than girls to be admitted to hospitals, and more women than men.

TABLE 5.—*Percentage Distribution According to the Patients' Sex of 2,178 Cases of Rheumatic Infection in Ten Cincinnati Hospitals During the Years 1930 to 1940, Based on Diagnosis at Initial Admission, Compared with 4,538 Cases in Philadelphia Hospitals from 1930 to 1934*

	Cincinnati Number of Cases	Percentage: Men and Boys		Percentage: Women and Girls	
		Cincinnati	Philadelphia	Cincinnati	Philadelphia
All rheumatic heart disease.	1,770	43	41	57	59
All rheumatic fever.....	583	54	50	46	50
All chorea.....	221	41	35	59	65
All rheumatic infections....	2,178	44	43*	56	57*
Chorea, uncomplicated.....	154	44	..	56	..
Chorea, complicated †.....	67	33	..	67	..

* An approximation derived by calculation from Hedley's tables.[2]

† By heart disease or rheumatic fever or both.

In a recent survey of 3,129 fatal cases, Cohn and Lingg [7] found the distribution between sexes equal. This was also approximately the condition observed in Cincinnati when only deaths were considered, for there were 191 among boys and men and 204 among girls and women. In Philadelphia there were 410 deaths in the former group and 506 in the latter.

RACIAL DISTRIBUTION OF CASES OF RHEUMATIC INFECTION

Analysis of the cases according to the patients' race shows that during the years 1930 through 1940 Negroes in Cincinnati had more than their share of this disease (table 6). Although Negroes were hospitalized for all causes in the same ratio as they appeared in the city's population, they had more than the expected amount of rheumatic fever and rheumatic heart disease and less chorea. Negroes comprised 10.6 per cent of the population in 1930 and 12.2 per cent in 1940, and in 11.5 per cent of all admissions to hospitals the patients were Negroes. Yet they accounted for 15 per cent of all the cases of rheumatic infection, 20 per cent of all deaths from rheumatic infection and 27 per cent of all cases of rheumatic fever with rheumatic heart disease. The last figure is two and one-half times as great as would be expected in relation to the number of admissions of Negroes to hospitals and to the proportion of Negroes in the population.

Surprisingly little information is available regarding the incidence of rheumatic infections in Negroes. From his survey of Philadelphia Hedley believed the disease to be "less common among Negroes than might be expected, considering their unfavorable economic circumstances as a result of which they are more likely to be hospitalized." [2] However, the present survey revealed that in Cincinnati the total number of admissions of Negroes to hospitals for all diseases was proportionate to the Negro population. Thus there was actually in this city a greater incidence of rheumatic infections in Negroes than the number in the population justified. This is also indicated in table 4, which shows the annual incidence of cases of hospitalization per hundred thousand of population to be 41.7 among white persons and 62.0 among Negroes. There is in this survey no support for the suggestion that "there is an apparent resistance among Negroes to rheumatic fever." [8b]

Chorea has been regarded as rare in Negroes. More recent reports indicate that, while it is less common in them than in white persons, it is by no means rare.[9] Negroes in Cincinnati comprised 11 per cent of the population and provided 8 per cent of the cases of chorea in which the patients were hospitalized (table 6).

TABLE 6.—*Percentage Distribution According to the Patients' Race of 2,178 Cases of Rheumatic Infection in Ten Cincinnati Hospitals from 1930 to 1940, Based on Diagnosis at Initial Admission, Compared with 4,538 Cases in Philadelphia Hospitals from 1930 to 1934*

	Cincinnati Number of Cases	Percentage: White		Percentage: Negro	
		Cincinnati	Philadelphia	Cincinnati	Philadelphia
All rheumatic heart disease.	1,770	85	87	15	13
All rheumatic fever.....	583	76	79	24	21
All chorea.....	221	92	94	8	6
All rheumatic infections....	2,178	85	86.5*	15	13.5*
City population (1930).....		89	89	11	11
All admissions (1930 through 1940)..		89	..	11	..

* An approximation derived by calculation from Hedley's tables.[2]

The distribution by race is analyzed in a different manner in table 7. There the chi square test is applied to determine the significance of the differences, it being assumed that the 326 cases in which the patients were Negroes and the 1,852 cases in which the patients were white persons represent random samples of the same population. The analysis shows that, within the

9. (*a*) Hedley.[2] (*b*) Lueth, H. C., and Sutton, D. C.: Chorea in the Negro Race, J. Pediat. **3**:775 (Nov.) 1933.

limits of the 2,178 cases, there were in Negroes, compared with white persons, much more rheumatic heart disease with rheumatic fever, more rheumatic heart disease with subacute bacterial endocarditis and more uncomplicated rheumatic fever than would be expected. There were in Negroes less uncomplicated rheumatic heart disease and less chorea than would be expected. In brief, rheumatic infection was more severe in Negroes.

DISTRIBUTION OF DEATHS BY AGE

In Cincinnati, of 2,178 cases of rheumatic infection, in 18.1 per cent the patient died as a result of the infection. In Philadelphia 20.2 per cent of the cases terminated fatally. In figure 2 there is given the percentage of the 395 fatalities in Cincinnati occurred within the ages of 40 to 49 years, although in Philadelphia it occurred at ages over 60.

TABLE 7.—*Distribution According to the Patients' Race of 2,178 Cases of Rheumatic Infection in Ten Cincinnati Hospitals from 1930 to 1940, Based on Diagnosis at Initial Admission*

	Total	White	Negro	χ^2
Rheumatic heart disease with rheumatic fever and subacute bacterial endocarditis	9	8	1	0.1
Rheumatic heart disease with subacute bacterial endocarditis	51	38	13	4.4*
Rheumatic heart disease with rheumatic fever and chorea	8	6	2	0.6
Rheumatic heart disease with rheumatic fever	312	226	86	38.9*
Rheumatic heart disease with chorea	52	48	4	2.2
Rheumatic heart disease, uncomplicated	1,338	1,178	160	9.5†
Rheumatic fever with chorea but no rheumatic heart disease	7	7	0	1.2
Rheumatic fever, uncomplicated	247	198	49	4.6*
Chorea, uncomplicated	154	143	11	7.4
Total rheumatic infections	2,178	1,852	326	68.9

* More than expected in Negroes.
† Less than expected in Negroes.
For $\chi^2 = 68.9$, $N = 8$, P is a very small number.

Cincinnati and 916 in Philadelphia which occurred in each age decade. The same trend is present as in the distribution of rheumatic heart disease by age groups. More of the deaths occurred in the older age groups in Cincinnati than in Philadelphia (fig. 2), just as more cases occurred in the older age groups in Cincinnati (fig. 1). In the former city, 65 per cent of the deaths occurred at ages above 30 years; in the latter, only 46 per cent. The mean age at death in Cincinnati was 36.2 years; in Philadelphia, 29.4 years. Roberts [10] found that the average age at death in Galveston, Texas, was 46 years.

When the number of deaths in each age decade is divided by the number of cases of rheumatic infections in the same decade, it is seen (fig. 3) that the highest case mortality in

10. Roberts, J. T., in discussion on Martin, A. T.: Twenty Years' Observation of 1.438 Children with Rheumatic Heart Disease, J. A. M. A. **117**:1663 (Nov. 15) 1941.

DISTRIBUTION OF DEATHS BY SEX AND RACE

Case mortality was lowest among white girls and women in both Cincinnati (15.3 per cent)

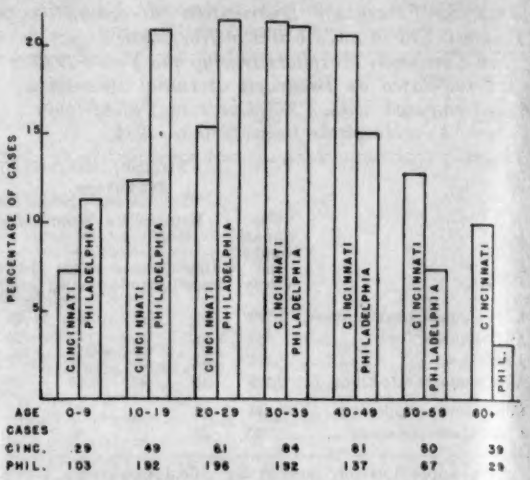

Fig. 2.—Percentage distribution by age decades of patients of 395 fatal cases of rheumatic heart disease, including 49 cases of subacute bacterial endocarditis superimposed on rheumatic heart disease, recorded in ten Cincinnati hospitals from 1930 to 1940, compared with 916 fatal cases in thirty-six Philadelphia hospitals from 1930 to 1934. Two other cases, for which the patients' ages are unknown, occurred in Cincinnati.

and Philadelphia (18.8 per cent) but highest among Negro girls and women (25.5 per cent and 23.2 per cent respectively) (table 8). This

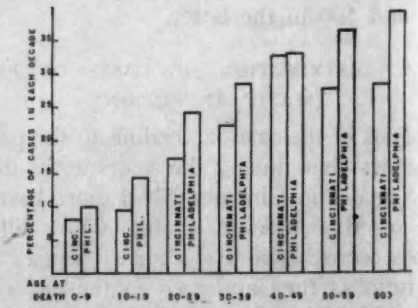

Fig. 3.—Case mortality by age decades; percentage of all cases of rheumatic infections in each age decade in which the patients died as a result of rheumatic heart disease in ten Cincinnati hospitals from 1930 to 1940 and in thirty-six Philadelphia hospitals from 1930 to 1934.

marked disparity did not exist between Negro and white boys or men. The death rate in Cincinnati among white children under 13 years of age was 6.6 per cent; among Negro children under 13 it was 14.4 per cent. These differences between races are probably caused in part by the presence in Cincinnati of adequate convalescent

facilities for white children and the absence of such facilities for Negro children.

According to Hedley,[11] a higher mortality from rheumatic heart disease is usual among Negroes aged 5 to 24 years. The mean age at death among white persons in Cincinnati was

TABLE 8.—*Case Mortality by Sex and Race Among 2,178 Cases of Rheumatic Infection in Ten Cincinnati Hospitals from 1930 to 1940 and Among 4,538 Cases in Philadelphia Hospitals from 1930 to 1934*

	White		Negro	
	Cincinnati	Philadelphia	Cincinnati	Philadelphia
Men and boys (%).....	19.3	21.2*	22.5	21.7*
Women and girls (%).....	15.3	18.8*	25.5	23.2*
All ages, both sexes (%)....	17.1	19.8	24.2	22.6
Under 13 yr., both sexes (%)	6.6	....	14.4	....
Mean age at death (yr.)....	33.2	29.8	28.6	27.1

* An approximation derived by calculation from Hedley's tables.[2]

38 years; among Negroes, 29. This compares with 30 and 27 respectively in Philadelphia. The mean age at death of 3,100 persons with rheumatic fever (primarily of the white race) in New York city was between 27 and 28 years.[12]

DAYS OF HOSPITAL CARE

In determining the number of days of hospitalization, only those cases were considered in which the patients were admitted primarily because of a rheumatic infection. There were 2,848 such admissions, representing 1,837 persons and 144,471 patient-days, or an average of fifty-one days for each admission for rheumatic infection. The comparable figure in Philadelphia was forty-six days. However, when convalescent facilities and children's hospitals were excluded, the average duration of hospitalization was twenty-three and thirty-five days in Cincinnati and Philadelphia respectively (table 9).

The patients in Cincinnati to whom convalescent care was given (white children aged 2 to 12 years) spent less time in hospital wards and more time in convalescent institutions for a combined longer period of care. An adequate number of beds was available for all children of this age range and racial group. Furthermore, the cost to the community per child is no greater than for a similar average child in Philadelphia institutionalized for a shorter period of time in a hospital ward, where the cost per patient-day is about twice that in a convalescent home.

All other groups of rheumatic patients, white adolescents and adults and all Negroes, received a shorter period of institutional care in Cincinnati than in Philadelphia. The costs of hospitalization and convalescent care have been discussed in previous publications.[13]

TABLE 9.—*Average Days of Hospital Care per Admission for Rheumatic Infection in Ten Cincinnati Hospitals from 1930 to 1940 and in Thirty-Six Philadelphia Hospitals from 1930 to 1934*

Hospitals	Rheumatic Heart Disease		Rheumatic Fever *		Chorea *		All Rheumatic Infections	
	Cincinnati	Philadelphia	Cincinnati	Philadelphia	Cincinnati	Philadelphia	Cincinnati	Philadelphia
General hospitals....	20	31	30	40	32	54	23	35
Children's hospitals.	41	60	47	59	39	53	42	59
All except convalescent hospitals.....	22	37	33	46	34	54	25	41
Convalescent hospitals †.....	253	‡	188	‡	201	‡	232	178
All hospitals.....	51	‡	43	‡	89	‡	51	46§

* With or without heart disease.
† Children's Heart Hospital (Philadelphia) and Children's Convalescent Home (Cincinnati).
‡ Unknown.
§ 267,509 patient-days divided by 5,801 admissions.[17]

COMMENT

A detailed comparison of the nature of the conditions of hospitalized patients with rheumatic infections in Cincinnati and in Philadelphia has been made. Because of the geographic and racial similarity of the two cities, no significant difference in the character of the rheumatic syndrome was anticipated. Contrary to expectations, certain definite differences were found. The most important of these can be summarized thus: In Cincinnati rheumatic infections were fewer and milder; they occurred less frequently in persons under the age of 34 years but more frequently in those over this age; the average age at death was almost seven years higher than in Philadelphia.

When the statistics were broken down according to race it was found that among Negroes of both cities the disease occurred about equally in persons up to the age of 34 years, after which the incidence in Cincinnati increased. It was only among young white persons that rheumatic infections were much less frequent in Cincinnati; in both races the incidence was greater in persons over the age of 34 years.

11. Hedley, O. F.: Trends, Geographical and Racial Distribution of Mortality from Heart Disease Among Persons 5 to 24 Years of Age in the United States During Recent Years (1922-1936), Pub. Health Rep. **54**:2271 (Dec. 29) 1939.

12. Cohn, A. E., and Lingg, C. M., cited by Swift, H. E.: The Nature and Etiology of Rheumatic Fever, Cincinnati J. Med. **23**:58 (April) 1942.

13. (*a*) Wedum, A. G., and Wedum, B. G.: Rheumatic Infections in Cincinnati Hospitals: I. Rheumatic Infections as a Hospital Problem, Cincinnati J. Med. **23**:489 (Dec.) 1942. (*b*) Wedum, B. G., and Wedum, A. G.: Rheumatic Infections in Cincinnati Hospitals: II. Convalescent Facilities and Needs, ibid. **23**:497 (Dec.) 1942.

This similarity in young Negroes and the difference in young white persons in the two cities should be accounted for by some factor operating for one of the race groups and not for the other. One is struck by the fact that adequate convalescent facilities have been available in Cincinnati since 1931 for all white children 2 to 12 years of age who required surgical or medical care, including the treatment of malnutrition. A large proportion of the patients cared for have had rheumatic infections. Such care was available for "only a small proportion of patients recovering from attacks of rheumatic fever" in Philadelphia.[2] Conversely, the older age groups of both races, in which rheumatic infections were more prevalent, have received less care, an average of only twenty-three days of institutionalization in Cincinnati compared with thirty-five in Philadelphia. These facts would seem to point to adequate care for young white persons with rheumatic infections in Cincinnati and inadequate care for Negro children and adults of both races as one explanation of the difference between the two cities.

This conclusion must be accepted with some caution. It may be, for some other reasons not yet clear, that the nature of the rheumatic syndrome is different in Cincinnati and in Philadelphia. For instance, another factor which may have contributed to the lesser severity among young white persons in Cincinnati is that an active program of vocational guidance for adolescents with rheumatic fever has been in operation there during the last fifteen years. Although such guidance has been available to members of both races, it is likely that it has operated to greater effect among white persons.[14] It is difficult to assess the influence of the difference in the intervals of time employed in the two surveys, 1930 to 1940 in Cincinnati and 1930 to 1934 in Philadelphia. In this connection, there are suggestions that rheumatic infections are becoming milder.[15] But in Cincinnati the number of hospitalized patients was increasing during the period studied.[15] Consequently, so far as can now be determined, the factors of convalescent care and length of time of institutionalization offer the hypothesis which most clearly and simply explains the observed differences.

The problem is a particularly important one at the present time. Rheumatic fever is surprisingly common among members of the armed forces.[16] The manner in which these young adults are handled will affect their individual futures and their significance in public health as a group. Persons with rheumatic infections which are neglected now will return to veterans' hospitals one or two decades hence as cardiac cripples. Our study tends to corroborate a growing conviction that care in a sanatorium or convalescent home, of proved value for children with rheumatic fever, should also be given to young adults.

SUMMARY

There was a total of 3,475 admissions of patients with rheumatic infections to all hospitals in Cincinnati for the period from Jan. 1, 1930 to Dec. 31, 1940. Analysis of the records of these admissions and comparison with similar data obtained in Philadelphia for the period from 1930 through 1934 revealed the following facts:

1. The rheumatic syndrome was more nearly the same in Negroes in the two cities than it was in white persons. Negroes constituted a considerably greater proportion of the patients with rheumatic heart disease with rheumatic fever and a somewhat smaller proportion of those with chorea than would be expected from their proportion in the population and in patients admitted to hospitals. Chorea is more common in Negroes than is generally realized.

2. In white persons in Cincinnati the incidence of rheumatic fever was lower, and the acute manifestations were less frequent, than in Philadelphia, and both morbidity and case mortality among children were lower. Among adults above the age of 35 years, the annual incidence of rheumatic heart disease per hundred thousand of population was greater in Cincinnati; this group accounted for more of the patients who died in Cincinnati than in Philadelphia. Adequate convalescent care for white children and comparatively inadequate length of hospitalization for adults in Cincinnati provide a possible explanation for these differences.

The data accumulated in this survey tend to corroborate the growing conviction that convalescent care, of proved value for children with rheumatic fever, should be given also to young adults. This concept is of major importance in handling rheumatic infections among young persons in military service.

The School of Medicine of the University of Colorado.

14. Schwartz, B. A.: Rheumatic Heart Disease of School Child, J. Med. **20**:425, 1939.

15. (*a*) Swift.[1] (*b*) Hedley.[11]

16. (*a*) Master, A. M.: Rheumatic Fever in the Navy, U. S. Nav. M. Bull. **41**:1019 (July) 1943. (*b*) Coburn, A. F.: Epidemiology of Streptococcus Hemolyticus Infections at Naval Training Stations, ibid. **41**: 1012 (July) 1943. (*c*) Unpublished data presented at a symposium in rheumatic fever, War-Time Graduate Medical Meeting, Fitzsimons General Hospital, Denver, Colo., Sept. 3, 1943.

17. Hedley,[2] p. 1614.

VITAMIN A ABSORPTION TEST IN CASES OF GIARDIASIS

LIEUTENANT (JG) CHRIS P. KATSAMPES (MC), U.S.N.R.;
AUGUSTA B. McCOORD, PH.D., AND WILLIAM A. PHILLIPS, M.D.*
ROCHESTER, N. Y.

The protozoan parasite Giardia lamblia, although frequently found in the stools and duodenal contents of children, has not been clearly demonstrated to be pathogenic for man. The varied and vague clinical symptoms associated with the presence of the parasites in the upper part of the small intestine in children have been adequately described by Véghelyi [1] and by Maris and Bushong.[2] The prompt and usually complete disappearance of the symptoms after successful expulsion of the parasite, particularly by the oral use of quinacrine hydrochloride,[3] as reported in recent years, is considered evidence in favor, but certainly not proof, of the pathogenicity of the parasite. In addition, Véghelyi [4] concluded indirectly, from the increased amount of fat and lipase in the stools of children with giardiasis, that the parasite impaired the absorption of fat from the intestines. The fact that after successful treatment of the infection the

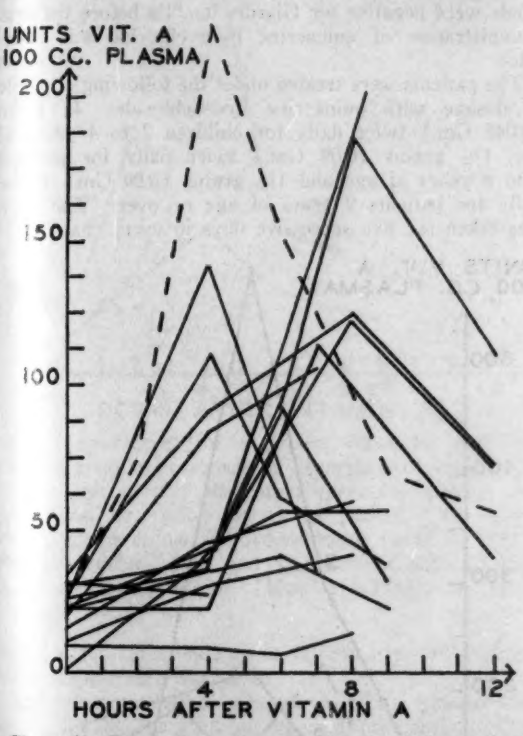

Chart 1.—Poor absorption of vitamin A by patients infected with Giardia lamblia before treatment with quinacrine hydrochloride. The normal absorption curve for vitamin A is represented by the broken line and curves obtained for the patients by solid lines.

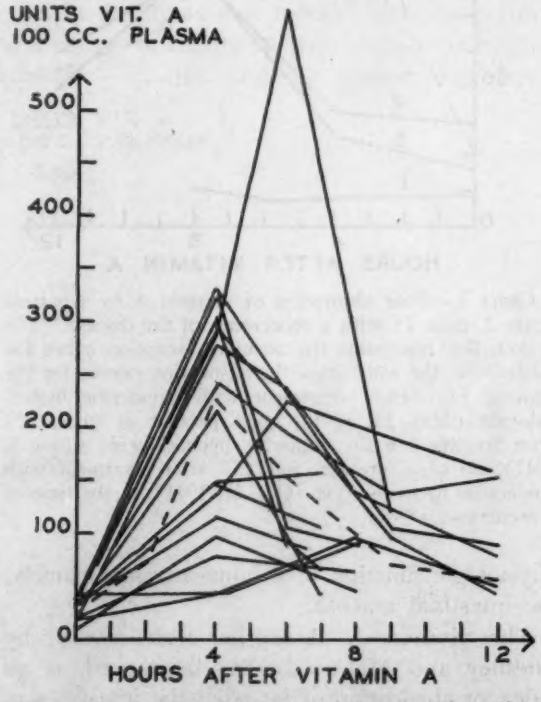

Chart 2.—Improved absorption of vitamin A by patients infected with Giardia lamblia after treatment with quinacrine hydrochloride. The normal absorption curve for vitamin A is represented by the broken line and curves for the patients by solid lines.

* Now Director Yuma County Public Health Unit, Yuma, Ariz.

From the Department of Pediatrics, University of Rochester School of Medicine and Dentistry.

1. Véghelyi, P.: Giardiasis in Children, Am. J. Dis. Child. **56**:1231 (Dec.) 1938.

2. Maris, E. P., and Bushong, S.: The Diagnosis of Giardia Intestinalis Infestation by Means of Intestinal Intubation: The Treatment with Atabrine and Follow-Up Studies of Sixty-Eight Cases, Pennsylvania M. J. **45**: 724 (April) 1942.

3. (*a*) Culbertson, J. T.: Specific Chemotherapy of Giardia Infections, J. Lab. & Clin. Med. **26**:1465 (June) 1941. (*b*) Hartman, H. R., and Kyser, F. A.: Giardiasis and Its Treatment: A Clinical Study, J. A. M. A. **116**:2835 (June 28) 1941. (*c*) Love, J., and Taylor, G. B.: Atabrine in the Eradication of Giardia Lamblia, U. S. Nav. M. Bull. **38**:239 (April) 1940.

4. Véghelyi, P.: Giardiasis, Am. J. Dis. Child. **59**: 793 (April) 1940.

amount of fat in the stools returned to normal levels indicated that removal of the parasite had permitted restoration of the normal power of the intestinal mucosa to absorb lipids. This has been the only objective evidence presented thus far of the ability of the parasite to disturb a normal

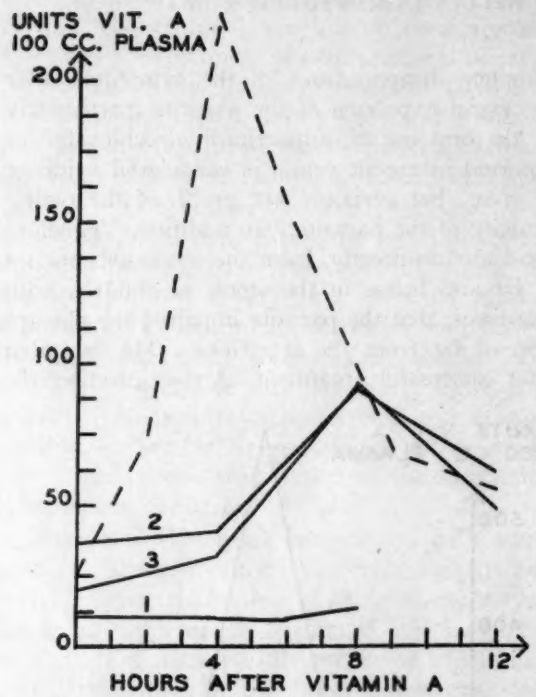

Chart 3.—Poor absorption of vitamin A by a patient (case 2, table 1) with a recurrence of the disease. The broken line represents the normal absorption curve for vitamin A; the solid lines, the absorption curves for the patient, (*1*) before treatment with quinacrine hydrochloride (May 15, 1941), cysts present in stool, (*2*) after treatment with quinacrine hydrochloride (June 3, 1941), no cysts present, and (*3*) after treatment with quinacrine hydrochloride (Oct. 17, 1941), at the time of a recurrence of cysts.

physiologic function of a human organ, namely, the intestinal mucosa.

The vitamin A absorption test, devised by Chesney and McCoord,[5] has been used as an index of absorption of fat from the intestines in celiac disease, catarrhal jaundice, tuberculosis and other diseases. In this study, the ability of the intestine to absorb fat in children with giardiasis, diagnosed by the detection of the parasite in their stools or duodenal contents, was determined by the vitamin A absorption test. The results obtained were compared with data obtained by repeated vitamin A absorption tests after expulsion of the parasites by treatment with the specific drug quinacrine hydrochloride.

5. Chesney, J., and McCoord, A. B.: Vitamin A of Serum Following Administration of Haliver Oil in Normal Children and in Chronic Steatorrhea, Proc. Soc. Exper. Biol. & Med. **31**:887 (April) 1934.

METHODS

The diagnosis of giardiasis was not considered established for the children studied unless the cysts of Giardia lamblia were found in their stools. In 10 cases trophozoites were obtained in the aspirated duodenal contents, but this confirmatory evidence is not considered requisite for the diagnosis if the cysts have been found in the stool. All except 3 of our subjects had the symptoms of the disease, and these symptoms disappeared when the parasites had been expelled.

The patient was concluded to be free of the parasites if after the third to the fifth day of treatment at least three stools obtained on successive days revealed no cysts. Whenever possible, examinations of stools for the cysts were done at intervals varying from one to seventeen months after treatment.

In the 3 control cases, consisting of 2 proved cases and 1 probable case of celiac disease, three or more stools were negative for Giardia lamblia before the oral administration of quinacrine hydrochloride was instituted.

The patients were treated under the following schedule of dosage with quinacrine hydrochloride: ¼ grain (0.045 Gm.) twice daily for children 2 to 4 years of age, 1½ grains (0.09 Gm.) twice daily for patients 5 to 8 years of age and 1½ grains (0.09 Gm.) thrice daily for patients 9 years of age or over. The drug was taken for five successive days in every case.

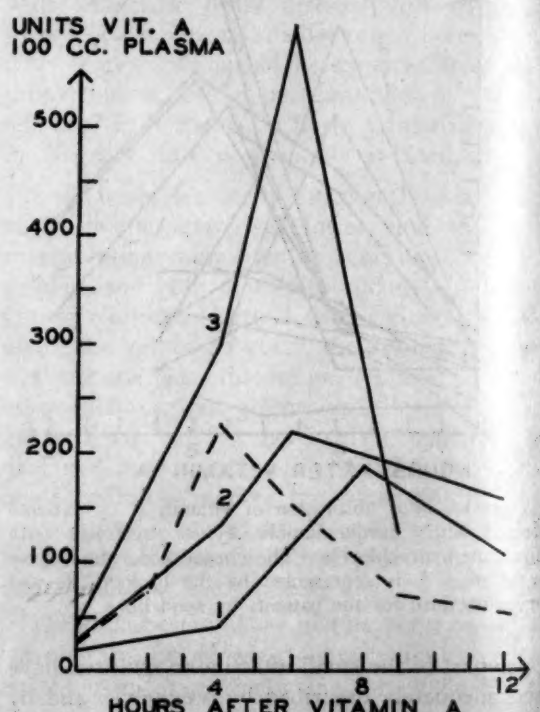

Chart 4.—Curves for the patient (case 3, table 1) showing most improvement in absorption of vitamin A. Broken line, normal absorption curve for vitamin A; solid lines, patient's absorption curves, (*1*) before treatment with quinacrine hydrochloride (June 3, 1941), cysts present in stool, (*2*) after treatment with quinacrine hydrochloride (July 10, 1941), no cysts present, and (*3*) after treatment with quinacrine hydrochloride (July 26, 1941), no cysts present.

The procedure followed in determining the absorption of vitamin A was that of Chesney and McCoord.[5] After a basal specimen of blood had been obtained, the child was given 7,000 U. S. P. units of vitamin A, in the

form of fish liver oil,[6] per kilogram of body weight, by mouth. The fish liver oil contained about 200,000 U. S. P. units of vitamin A per gram. A specimen of blood was taken four hours later and usually at several subsequent intervals during the next eight hours, and the concentration of vitamin A in the samples was determined, as is shown in the tables. During the test, the

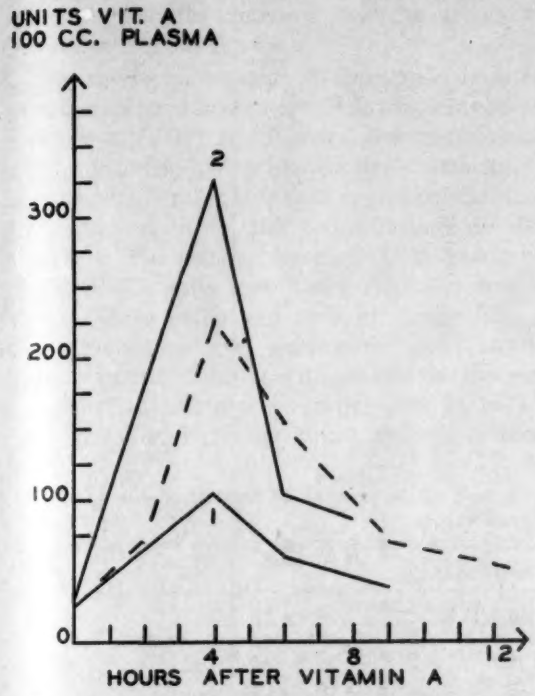

Chart 5.—Curves for a patient (case 13, table 1) showing great improvement in absorption of vitamin A. Broken line, normal absorption curve for vitamin A; solid lines, absorption curves of patient, (*1*) before treatment with quinacrine hydrochloride (May 11, 1943), cysts present in stool, and (*2*) after treatment with quinacrine hydrochloride (May 21, 1943), no cysts present.

child ate the usual meals, but no cod liver oil or vitamin A supplement was given.

The concentration of vitamin A in the plasma was determined by the method reported previously.[7] One of the units in which the results are recorded equals about 3.8 U. S. P. units of vitamin A. The carotenoids, carotene and xanthophyll of the plasma were determined according to the method of Clausen and McCoord.[8] Since there were no significant changes in the carotenoids during the course of our studies, the values obtained are not reported in the tables.

In our cases treatment with quinacrine hydrochloride was commenced as soon as the diagnosis of giardiasis was established and the first vitamin A absorption test was completed. Since in our patients the amount of fat in the stools and the dextrose tolerance were essentially normal, the data for these are not reported.

6. Dr. Carl Nielsen, of the Abbott Laboratories, supplied the fish liver oil used in these tests.

7. Clausen, S. W.; Baum, W. S.; McCoord, A. B.; Rydeen, J. O., and Breese, B. B.: Mobilization by Alcohols of Vitamin A from Its Stores in the Tissues, J. Nutrition **24**:1 (July) 1942.

8. Clausen, S. W., and McCoord, A. B.: The Determination of Carotene and Xanthophyll by a Single Distribution Between Liquid Phases, J. Biol. Chem. **113**:89 (Feb.) 1936.

RESULTS

In only 3 of 15 cases studied, data on which are shown in table 1, were none of the symptoms commonly attributed to the parasitic infestation present. In these 3 cases, Giardia lamblia cysts were found during routine examination of stools for other purposes, whereas in the cases in which the symptoms were evident the clinical symptoms and signs led to a search for the cysts. The asymptomatic patients could be considered as carriers or as being in a latent stage of the disease. The remaining 12 patients had symptoms fitting closely into the clinical picture described by Véghelyi. In 12 cases, after the patient had received one five day course of treatment with quinacrine hydrochloride orally the symptoms disappeared completely within one week. In only 1 case (no. 2, table 1) to our knowledge did a recurrence, or more probably a relapse, occur, with a return of clinical symptoms and of the cysts in the stools four months after completion of a course of treatment with quinacrine hydrochloride. In this case the patient was given

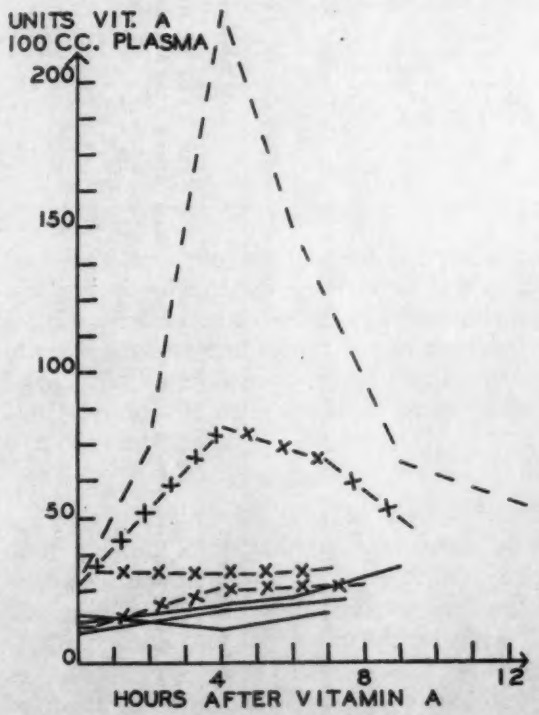

Chart 6.—Poor absorption of vitamin A by patients with celiac disease before and after treatment with quinacrine hydrochloride. Broken line, normal absorption curve for vitamin A; solid lines, curves for patients before treatment with quinacrine hydrochloride; lines with crosses, curves after treatment with quinacrine hydrochloride.

another course of treatment, resulting in disappearance of clinical symptoms and of the cysts from the stools, but unfortunately the case could not be followed thereafter for a possible per-

TABLE 1.—*Absorption of Vitamin A by Patients Infected with Giardia Lamblia Before and After Treatment with Quinacrine Hydrochloride*

		Units of Vitamin A per 100 Cc. of Plasma																					
		Before Treatment							After Treatment, First Test								After Treatment, Second Test						
Patient No.	Date of Test	Basal	4 Hr. After A	6 Hr. After A	7 Hr. After A	8 Hr. After A	9 Hr. After A	12 Hr. After A	Date of Test	Basal	4 Hr. After A	6 Hr. After A	7 Hr. After A	8 Hr. After A	9 Hr. After A	12 Hr. After A	Date of Test	Basal	4 Hr. After A	6 Hr. After A	8 Hr. After A	9 Hrs. After A	12 Hr. After A
1	5/ 7/41	11	30	..	..	40	..	..	5/16/41	7	98	..	..	42	..	..	10/ 3/42	18	323	..	141	..	78
2	5/15/41	9	8	6	..	13	..	..	6/ 3/41	36	40	..	..	93	..	60	10/17/41	19	31	..	95	..	48
3	6/ 3/41	20	37	..	..	184	..	108	7/10/41	28	132	219	..	..	..	34 (24 Hr.)	7/26/41	37	297	582	..	126	..
4	10/22/41	34	91	..	..	124	..	70	.....	..	..	..	..	..	..	..	.....	..	..	..	..	..	..
5	11/ 4/41	29	38	..	..	122	..	70	10/24/42	22	79	..	..	65	..	..	.....	..	..	..	..	..	..
6	2/18/42	2	38	92	..	..	31	..	10/17/42	27	238	193	..	..	133	152	.....	..	..	..	..	..	..
7	3/26/42	24	44	56	..	..	56	..	1/ 9/43	18	304	88	..	..	..	..	.....	..	..	..	..	..	..
8	4/ 4/42	23	35	41	..	..	22	..	.....	..	..	..	..	..	..	..	.....	..	..	..	..	..	..
9	6/ 1/42	22	22	..	118	..	..	38	6/11/42	28	271	230	..	..	109	87	10/31/42	13	116	299	..	97	70
10	9/ 9/42	14	45	..	..	58	..	..	.....	..	..	..	..	..	..	..	.....	..	..	..	..	..	..
11	5/ 5/43	32	27	..	..	..	..	..	5/11/43	33	139	..	104	..	..	..	.....	..	..	..	..	..	..
12	5/ 7/43	20	83	..	104	..	..	..	5/14/43	27	146	..	156	..	..	..	.....	..	..	..	..	..	..
13	5/11/43	25	109	60	..	..	37	..	5/21/43	26	325	109	..	87	..	..	.....	..	..	..	..	..	..
14	7/ 1/43	25	34	93	..	..	255	..	7/ 9/43	32	113	85	69	..	..	..	.....	..	..	..	..	..	..
15	8/ 5/43	25	139	..	35	..	..	..	9/10/43	22	216	..	37	..	..	..	.....	..	..	..	..	..	..

sistence or recurrence of the disease. In every instance Giardia lamblia cysts rapidly disappeared from the stools after the third day of treatment with quinacrine hydrochloride, and, with the exception just mentioned, repeated examinations over a period ranging from one to seventeen months showed that the stools remained free from the cysts.

The results of vitamin A absorption tests for the 15 children infected with Giardia lamblia are given in table 1. In all cases, before treatment with quinacrine hydrochloride these patients did not absorb vitamin A as well as normal children. In normal children, the concentration of vitamin A in the plasma increases to a maximum of about 225 units four hours after the dose of vitamin A is given and then gradually falls to about the basal level during the next twenty hours. In the children with giardiasis, the concentration of vitamin A varied from 8 to 139 units at the end of four hours, though in some cases somewhat higher values were obtained several hours later.

The relative flatness of these curves of absorption and the delay in reaching the maximum value as compared with the normal curve for vitamin A absorption are shown more clearly in chart 1. The normal curve for vitamin A absorption represents the average values obtained for 12 normal children.[5]

As is shown in table 1, for 12 of these patients the first test of vitamin A absorption was carried out from one day to one year after the treatment with quinacrine hydrochloride. All of these patients showed improved absorption of the vitamin, and in many cases the maximum concentration of vitamin A in the plasma was found at the expected time, four hours after the administration of the vitamin. In some cases the patients then were able to absorb the vitamin even better than average normal children. These results are shown graphically in chart 2.

For 4 of these children, a second test of vitamin A absorption after treatment with quinacrine hydrochloride gave essentially the same results. However, it is interesting to note that 1 child (case 2, table 1) who had a recurrence of the disease still showed relatively poor absorption of the vitamin. His absorption curves are shown in chart 3. On the other hand, the great improvement shown by 2 other patients (cases 3 and 13) is represented in charts 4 and 5.

We felt, however, that it was desirable to determine whether the administration of quinacrine hydrochloride had a direct effect on the absorption of vitamin A by children. Accordingly, we selected 3 patients with celiac disease but free from giardiasis and subjected them to the same course of treatment with quinacrine hydrochloride that the patients with giardiasis received. The results obtained are shown in table 2 and chart 6. As is characteristic in celiac disease, the initial tests of these children showed poor absorption of vitamin A. After treatment with quinacrine hydrochloride, only 1 patient (case 2, table 2) showed much improvement, and this may have been due to the fact that the first test was performed on the day on which she was admitted to the hospital and the second test after she had been receiving for eight days a more carefully controlled diet for the treatment of celiac disease than she had been receiving at home. We concluded, therefore, that quinacrine hydrochloride has no direct effect on the absorption of vitamin A.

TABLE 2.—*Absorption of Vitamin A by Patients with Celiac Disease Before and After Treatment with Quinacrine Hydrochloride*

		Units of Vitamin A per 100 Cc. of Plasma									
		Before Treatment					After Treatment				
Patient No.	Date of Test	Basal	4 Hr. After A	6 Hr. After A	7 Hr. After A	9 Hr. After A	Date of Test	Basal	4 Hr. After A	7 Hr. After A	8 Hr. After A	9 Hr. After A
1	2/17/43	10	17	..	21	..	3/25/43	12	25	..	27	..
2	7/15/43	13	18	22	..	33	7/23/43	20	79	70	..	49
3	9/16/43	14	8	..	14	..	10/ 5/43	32	30	32	..	..

SUMMARY

Since infection with Giardia lamblia in children seriously interfered with the absorption of vitamin A and in all probability with the absorption of other fat-soluble vitamins as well, we are of the opinion that this organism is pathogenic in children. After the parasites were eliminated by treatment with quinacrine hydrochloride, the health of patients with giardiasis and the ability of such patients to absorb vitamin A were much improved. In control patients with celiac disease, treatment with quinacrine hydrochloride did not affect the absorption of vitamin A.

Dr. S. W. Clausen gave us the opportunity to carry out this study and gave advice on the work.

University of Rochester School of Medicine and Dentistry.

Yuma County Public Health Unit.

INFLUENZAL MENINGITIS

McLEMORE BIRDSONG, M.D.; W. W. WADDELL JR., M.D.,
AND BETTY W. WHITEHEAD, M.D.
CHARLOTTESVILLE, VA.

Meningitis caused by strains of Haemophilus influenzae is one of the types of meningitis prevalent in children. Until recently treatment was unsatisfactory and the mortality high. Prior to the advent of type-specific anti-influenzal rabbit serum the mortality varied from 65 to 100 per cent.

Six strains of H. influenzae have been described: a, b, c, d, e and f. Pittman in 1931 emphasized the fact that type b H. influenzae was the strain most commonly causing this type of meningitis. We have observed 1 case of severe meningitis caused by type f H. influenzae.

Alexander, Ellis and Leidy [1] in an excellent article on H. influenzae infections outlined the biologic characteristics of the organisms and presented a method of treatment similar to the method described in this report.

Before the use of specific serum all patients admitted to the pediatric service of the University of Virginia Hospital with influenzal meningitis died. With the advent of chemotherapy the period of morbidity was prolonged from an average of seven days to an average of twelve days. We are unable, however, to report a single case of recovery resulting from chemotherapy alone. The first patient treated with type-specific anti-influenzal rabbit serum was admitted to the hospital in May 1940. Since that time we have used serum in 8 cases, which are reported here.

REPORT OF CASES

CASE 1.—M. C., a 4 year old white girl, was admitted to the hospital with symptoms of high fever, nausea, vomiting and headache of three days' duration. Her past history was noncontributory.

Physical examination revealed a well developed child, lying quietly in bed, apparently acutely ill. Her temperature was 104 F., her pulse rate 128 and her respiratory rate 28. The cutaneous turgor was poor. The pharynx was moderately injected, and the anterior cervical nodes were enlarged. The neck was stiff, and the Kernig sign was questionable.

Laboratory Data.—The hemoglobin content and red cell count of the blood were normal. There were 28,600 white cells per cubic millimeter of blood, with a normal differential count. The carbon dioxide-combining power of the blood was 35 volumes per cent, and the level of the blood sugar was normal. Wassermann and Kahn tests of the blood gave negative results. The urine was normal.

The spinal fluid was cloudy and under increased pressure. There were 7,800 cells per cubic millimeter, of which 95 per cent were polymorphonuclear leukocytes. The fluid contained 200 mg. of protein per hundred cubic centimeters and sugar was absent. Smears revealed organisms at first thought to be meningococci but later identified as H. influenzae. Culture showed type b H. influenzae.

Course and Treatment.—The patient was immediately given 630 cc. of a sixth molar solution of sodium lactate to combat dehydration and acidosis. Because of the first impression that the spinal fluid contained meningococci, 20,000 units of meningococcus antiserum was given intramuscularly. Sulfanilamide was given subcutaneously. On the second day the cultures of the spinal fluid were reported as containing type b H. influenzae. The child was then given an initial dose of sulfathiazole sodium intravenously, and administration of this drug was continued by mouth. Satisfactory levels were maintained by this method. On the patient's third day in the hospital 25 mg. of type b H. influenzae rabbit serum was given intramuscularly in the morning and another dose of 25 mg. that evening. This treatment was followed by the first real evidence of improvement. On the fourth day the agglutination of organisms from the patient's spinal fluid by her blood serum was moderate. Twenty-five milligrams of serum was given that day and again on the fifth day. By this time the number of cells in the spinal fluid had dropped to 137 per cubic millimeter, and a culture of the fluid was sterile. The child was greatly improved by the seventh day. The administration of sulfathiazole was discontinued on the twelfth day. Subsequent cultures of the spinal fluid were sterile. Except for having a few unexplained rises in temperature the child made an uneventful recovery and was discharged after one month in the hospital.

CASE 2.—A. A., a 3 year old Negro girl, was well except for a slight cold in the head until eighteen hours before admission to the hospital, when she became stuporous and began to have intermittent convulsive movements of the arms and legs.

Physical examination revealed a well developed child who was stuporous and was having generalized convulsive movements. Her temperature was 105 F., the pulse rate 140 and the respiratory rate 40. The skin

From the Department of Pediatrics, University of Virginia Hospital.

1. Alexander, H. E.; Ellis, C., and Leidy, G.: Treatment of Type-Specific Hemophilus Influenzae Infections in Infancy and Childhood, J. Pediat. **20**: 673-698 (June) 1942.

was hot and dry. A purulent nasal discharge was present. The pharynx was injected, and the tonsils were moderately hypertrophied. The neck and spine were stiff, and the Kernig and Brudzinski sign were positive.

Laboratory Data.—The hemoglobin content and erythrocyte count of the blood were normal. There were 46,200 white cells per cubic millimeter of blood with 86 per cent of polymorphonuclear leukocytes. The Wassermann and Kahn reactions of the blood were strongly positive on several occasions. The urine was normal, and the cutaneous reaction to tuberculin was negative. The blood culture contained type b H. influenzae.

The spinal fluid was cloudy and under increased pressure. It contained 200 mg. of protein, 34 mg. of sugar and 700 mg. of chlorides per hundred cubic centimeters. The cell count was 600 per cubic millimeter with 60 per cent polymorphonuclear leukocytes. Smears revealed a gram-negative pleomorphic organism, which was later typed from culture and proved to be type b H. influenzae. The Wassermann reaction of the spinal fluid was strongly positive, and the colloidal gold curve was 4333553211.

Course and Treatment.—The administration of sulfadiazine was started immediately by mouth. On the second day there was no improvement, and a second lumbar puncture was done. The number of cells per cubic millimeter of spinal fluid had increased to 3,830 with 98 per cent polymorphonuclear leukocytes. By this time the organism had been identified as type b H. influenzae. Fifty milligrams of type-specific rabbit serum was given intravenously. Twenty-five milligrams of serum was given on the third day and again on the sixth day. The agglutination of the organisms from the spinal fluid of the patient by her blood serum was good on the third day, and clinical improvement was noted at that time. By the seventh day the patient seemed much better. Her spinal fluid contained 117 cells per cubic millimeter, with 75 per cent polymorphonuclear leukocytes and a culture was sterile. Subsequent cultures of the spinal fluid were sterile. Sulfadiazine therapy was discontinued on the nineteenth day. During the period of convalescence antisyphilitic therapy was begun. The child was discharged from the hospital on the twenty-first day with no demonstrable sequelae.

Case 3.—E. W., a 7 year old white girl, was admitted to the hospital with a history of headache of two days' duration, accompanied by photophobia, nausea and vomiting. On the day before admission she became extremely listless and appeared to have become deaf.

Physical examination revealed a fairly well developed but poorly nourished white girl who was extremely ill and semicomatose. Her temperature was 101.2 F., the pulse rate 100 and the respiratory rate 26. She was moderately dehydrated. There was a profuse anterior and posterior nasal discharge. The neck was stiff, and the Kernig sign was positive.

Laboratory Data.—The hemoglobin content and erythrocyte count of the blood were normal. There were 21,000 white cells per cubic millimeter of blood with 89 per cent polymorphonuclear leukocytes. The urine, the cutaneous reaction to tuberculin and the reaction of the blood to Wassermann and Kahn tests were all normal, and the blood culture was sterile.

The spinal fluid was cloudy and under increased pressure. It contained 120 mg. of protein, 705 mg. of chlorides and 25 mg. of sugar per hundred cubic centimeters. The cell count was 3,800 with 98 per cent polymorphonuclear leukocytes. A smear showed gram-negative bacilli which proved on direct typing to be type b H. influenzae.

Course and Treatment.—The patient was immediately given an intravenous infusion of isotonic solution of sodium chloride with 5 per cent dextrose to combat dehydration. In the meantime influenza bacilli were typed from the spinal fluid, and 25 mg. of type-specific rabbit serum was then given intravenously. Sulfadiazine was administered by mouth in adequate dosage. A second dose of 25 mg. of serum was given at the end of twenty-four hours. On the second day the patient seemed improved, but the number of cells in the spinal fluid had risen to 5,200 per cubic millimeter. On the third day the cell count had decreased to 1,200. A third dose of 25 mg. of serum was given. At this time agglutination of the organisms from the patient's spinal fluid by her serum was slight. She continued to improve, and by the fifth day the agglutination reaction was moderate. The cell count for the spinal fluid was then down to 204 with 66 per cent lymphocytes. Culture of the spinal fluid showed no organisms. The child was discharged from the hospital on the sixteenth day, well except for the deafness which was noted on admission.

Case 4.—R. D., a 9 month old white boy, was admitted to the hospital with a history of a cold of one week's duration, anorexia, vomiting and fever of three days' duration and a stiff neck of one day's duration. At the beginning of the illness the patient was convalescing from whooping cough.

Physical examination revealed a well developed 9 month old child who appeared acutely ill. The temperature was 104.4 F. The anterior fontanel was full and tense. Both ear drums were red but not bulging. There was a serous nasal discharge, and the pharynx was moderately injected. The neck was stiff, and the Kernig and Brudzinski signs were positive.

Laboratory Data.—The hemoglobin content and erythrocyte count of the blood were normal. There were 39,400 white cells per cubic millimeter, with a normal differential count. The urine, the reaction of the blood to the Wassermann test and the cutaneous reaction to tuberculin were normal. Cultures of the blood contained type b H. influenzae.

The spinal fluid was clear and contained 100 mg. of protein, 15 mg. of sugar and 660 mg. of chlorides per hundred cubic centimeters. The cell count was 597, with 70 per cent polymorphonuclear leukocytes. No organisms were seen in a direct smear, but a culture revealed type b H. influenzae.

Course and Treatment.—On admission to the hospital the child was immediately given sulfadiazine by mouth. The course of the illness was stormy, with a temperature ranging around 103 F. to 104 F. Lumbar punctures were done daily. Organisms were not found until the initial culture had been incubated for five days. They were then identified in both the blood and the spinal fluid as type b H. influenzae. As soon as this information was obtained the child was given 50 mg. of type-specific rabbit serum intravenously. Agglutination of the organisms from the spinal fluid by blood serum from the patient was moderately positive the next day. On subsequent days this reaction was about the same. By the patient's eighth day in the hospital the temperature had returned to normal, and the remainder of the course was uncomplicated. After two sterile cultures of spinal fluid had been obtained, the child

was discharged in good condition on the twenty-third hospital day. There were no sequelae.

CASE 5.—R. H., an 18 month old white boy, was admitted to the hospital with a history of a cold, listlessness and fever of five days' duration. On the day before admission his drowsiness gradually increased until he was in a stuporous condition.

Physical examination revealed a well developed, acutely ill white boy. The temperature was 102.4 F. The skin was dry with poor turgor. The neck was not stiff, but the Brudzinski and Kernig signs were positive.

Laboratory Data.—The erythrocyte count was 3,800,000 per cubic millimeter and the hemoglobin content of the blood was 65 per cent. There were 15,600 white cells per cubic millimeter of blood with 76 per cent polymorphonuclear leukocytes. Urinalysis, a cutaneous tuberculin test and a Wassermann test of the blood gave normal results.

The spinal fluid was purulent and under increased pressure. It contained 100 mg. of protein, 7 mg. of sugar and 600 mg. of chlorides per hundred cubic centimeters. The cell count was 38,000, with 97 per cent polymorphonuclear leukocytes. A smear revealed many gram-negative bacilli which were typed directly and identified as type b H. influenzae.

Course and Treatment.—Soon after the patient was admitted to the hospital a continuous intravenous drip was started with isotonic solution of sodium chloride. As soon as the organism was identified in the spinal fluid 25 mg. of type-specific rabbit serum was given. Six hours later this dose was repeated. At this time the child was also given an initial dose of sodium sulfadiazine through the drip infusion. The administration of sulfadiazine was then continued by mouth. On the second day some improvement in the child's clinical appearance was noted. An additional 25 mg. of type-specific antiserum was given. In spite of this rather vigorous treatment the patient's condition did not continue to improve satisfactorily, and his temperature remained between 101 F. and 103 F. On the fourth day both ear drums were found to be buiging, and bilateral myringotomy was performed. Culture of pus from the ears revealed the presence of type b H. influenzae. At this time the organisms from the patient's spinal fluid were not agglutinated by his blood serum. The number of cells in the spinal fluid had fallen to 3,950 per cubic millimeter, but the smear still showed numerous organisms. Because of these findings another dose of 50 mg. of type-specific antiserum was given. Generalized erythema with urticaria developed immediately, and respiration became labored. The condition was relieved by the administration of epinephrine. After this series of events the condition of the patient improved. He became afebrile on the following day and began to take fluids and food well. After four sterile cultures of spinal fluid were obtained the patient was discharged from the hospital in good condition one month after admission.

CASE 6.—A. D., a 3 year old Negro girl, was admitted to the hospital with a history of fever, vomiting and drowsiness of three days' duration and delirium of one day's duration. The past history was important in that she had appeared mentally retarded since early childhood.

Physical examination revealed a well developed but thin child who appeared delirious and acutely ill. The temperature was 103.9 F., the pulse rate 120 and the respiratory rate 32. The skin was hot and dry. There was a slight strabismus; the neck was stiff, and the Kernig and Brudzinski signs were positive.

Laboratory Data.—The hemoglobin content and the erythrocyte count of the blood were normal. There were 13,000 white cells per cubic millimeter. The urinalysis, cutaneous tuberculin test and blood Wassermann test gave normal results. Cultures of the blood contained type b H. influenzae.

The spinal fluid was purulent and under increased pressure. It contained 100 mg. of protein and 705 mg. of chlorides per hundred cubic centimeters, and no sugar. There were 28,000 white cells per cubic millimeter, with 98 per cent polymorphonuclear leukocytes. Type b H influenzae was typed directly and grown in a culture of spinal fluid.

Course of Treatment.—Soon after the child was admitted to the hospital she was given 50 mg. of type-specific rabbit serum and sulfadiazine was administered by mouth. On the second hospital day there was only slight agglutination of the organisms from the spinal fluid of the patient by her serum. Another 50 mg. dose of serum was given. Although the child looked somewhat improved, her temperature remained elevated, and the cultures of the spinal fluid continued to show organisms until her eighth day in the hospital. Because the agglutination reaction was still negative, a final dose of 50 mg. of serum was given on the sixteenth day. Three sterile cultures of spinal fluid were then obtained; the temperature remained normal, and the general course was thereafter uneventful. The child was discharged from the hospital five weeks after admission. She appeared weak, her gait was unsteady and she showed a slow mental response. There was some question as to whether these symptoms were due to her previous mental deficiency or were associated with her illness.

CASE 7.—L. S., a 2 year old white girl, was admitted to the hospital with a history of irritability and fever of four days' duration and stiffness and soreness of the neck of one day's duration. Just prior to her admission she had been taken to her family physician, who had done a spinal tap and had found that the fluid contained 1,404 cells per cubic millimeter and gram-negative bacilli evident in a direct smear. He gave the patient 1 Gm. of sodium sulfadiazine intravenously and 30 cc. of "Lyovac" H. influenzae antiserum.

Physical examination revealed a well developed 2 year old white girl who did not seem acutely ill. Her temperature was 103.4 F. The neck and spine were stiff and were held in opisthotonos position. The Kernig and Brudzinski signs were positive.

Laboratory Data.—The hemoglobin content and the erythrocyte count of the blood were normal. There were 9,200 white cells per cubic millimeter of blood, with 75 per cent polymorphonuclear leukocytes. The urinalysis and Wassermann test gave normal results.

The spinal fluid was cloudy and under increased pressure. It contained 45 mg. of protein, 66 mg. of sugar and 720 mg. of chloride per hundred cubic centimeters. The content of sulfadiazine was 4 mg. per hundred cubic centimeters. There were 1,950 white cells per cubic millimeter, 85 per cent of which were polymorphonuclear leukocytes. A smear showed gram-negative bacilli which were later identified by culture and typing as type b H. influenzae.

Course and Treatment.—As soon as the organism in the spinal fluid had been identified, sulfadiazine therapy was started by mouth and 50 mg. of type-specific rabbit serum was given intravenously. Twenty-five milligrams of serum was given daily for the next three days. Clinical improvement was noted by the third day. Agglutination of the organisms from the patient's spinal fluid by her serum was slight on the third day and on the fifth day. The temperature returned to normal by the fifth day, and the spinal fluid at that time showed only 89 cells per cubic millimeter and gave a sterile culture. Two additional sterile cultures were obtained before the patient was discharged. On the seventh day in the hospital the patient's urinary output became extremely small, and she began to complain of pain in the lower part of the abdomen. Catheterization revealed that there was little urine in the bladder, and the urine which was obtained contained innumerable crystals of sulfadiazine and many red blood cells. With the help of cystoscopy and the intravenous administration of large amounts of isotonic solution of sodium chloride, the obstruction was relieved, and the renal function returned to normal. The course of the rest of the illness was uneventful except for a brief episode of otitis media which subsided without any complications. The child was discharged in good condition, without evidence of sequelae.

Case 8.—J. L., a 3½ months old white child, was seen in the outpatient department on the day before he was admitted to the hospital with a history of an infection of the upper respiratory tract of five days' duration and fever of two days' duration. Examination at that time revealed both ear drums to be bulging, but no other abnormal physical conditions were observed. A bilateral myringotomy was performed, and pus was obtained. The child was sent home and given sulfadiazine, and he was to be brought back the following day. The next day he was brought back unimproved. His temperature was 102.4 F., and both ears were draining. He was then admitted to the ward.

Physical examination on admission revealed a well developed 3½ month old white infant who was having clonic convulsive movements of the extremities. The eyes were deviated to the right. The temperature was 102.6 F. The anterior fontanel was tense and pulsating. There was purulent drainage form both ears. Stiffness of the neck was only slight, but the Kernig and Brudzinski signs were positive.

Laboratory Data.—The erythrocyte count was 3,800,000 and the hemoglobin content 65 per cent. There were 8,900 white cells per cubic millimeter of blood, with 59 per cent polymorphonuclear leukocytes. Urinalysis and a Wassermann test of the blood showed no abnormality.

The spinal fluid was extremely cloudy and under increased pressure. It contained 350 mg. of protein and 695 mg. of chlorides per hundred cubic centimeters and no sugar. There were 15,500 cells per cubic millimeter, with 84 per cent polymorphonuclear leukocytes. A smear showed a moderate number of gram-negative pleomorphic bacilli, which proved to be type b H influenzae.

Course and Treatment.—Immediately after the child was admitted to the hospital a drip infusion into the bone marrow was started with isotonic solution of sodium chloride, and sodium sulfadiazine was given by this route. In the meantime the organism in the spinal fluid was identified and 50 mg. of type-specific rabbit serum was given. The following morning the child still seemed to be in a critical condition and remained semicomatose, with occasional convulsive movements. He was given 25 mg. of type-specific serum, and a second spinal tap was done. The fluid now contained 37,600 cells per cubic millimeter, with 94 per cent polymorphonuclear leukocytes. The child's condition continued to grow worse, and he died twenty-one hours after admission to the hospital. Autopsy was not permitted.

COMMENT

An outline of the therapy employed in this short series of cases follows. As soon as the diagnosis of H. influenzae meningitis was established the administration of sulfadiazine was started, usually intravenously. If dehydration was present it was treated by intravenous or bone marrow Murphy drip infusion. By the time dehydration had been corrected and chemotherapy was well established, the organism usually had been typed and specific serum could be given. Type-specific H. influenzae rabbit serum was used intravenously. An initial dose of 50 mg. seemed most satisfactory. The need for further serum therapy was determined by the clinical condition of the patient, the bacterial content, the cell count and sugar content of the spinal fluid and the agglutination response of the organisms cultured from the spinal fluid with the patient's blood serum. This reaction is tested as follows: Toward one end of a slide a loopful of a suspension of organisms cultured from the patient's blood or spinal fluid and a loopful of the patient's serum are placed. These are mixed and spread out in a rather thin smear. On the other end of the slide a loopful of the suspension of organisms and a loopful of isotonic saline solution (or normal serum) are placed. These are mixed and a thin smear is made. The smears are stained with alkaline methylene blue (diluted several times to prevent overstaining of the serum) and examined microscopically for evidence of agglutination of the organisms. In our experience moderate agglutination is evidence of adequate serum therapy.[2]

Sulfadiazine was administered by mouth in doses of 1 to 1½ grains (0.06 to 0.09 Gm.) per pound (0.5 Kg.) of body weight per day as long as there was any evidence of active infection. A blood level of 8 to 12 mg. per hundred cubic centimeters was considered satisfactory. The condition of the urine was observed closely for

2. Bray, W. E.: Synopsis of Clinical Laboratory Methods, ed. 2, St. Louis, C. V. Mosby Company, 1938, p. 260.

evidence of renal complications. Lumbar punctures were done at frequent intervals until the spinal fluid became clear.

In case 4 it will be noted that the diagnosis was late, the patient having been treated initially for meningococcic meningitis. The diagnosis was finally established by finding H. influenzae in the blood culture. It is important that blood cultures be made in all cases of suspected meningitis. In case 4 it will also be noted that there was no response to adequate chemotherapy. Prompt improvement followed the administration of serum.

Case 5 illustrates the importance of careful and frequent examination of the ears. It has been reported by others that the presence of otitis media in patients with influenzal meningitis is correlated with a higher mortality. In this particular case improvement was rapid after myringotomy was performed.

The high incidence of recovery in this small series of cases of H. influenzae meningitis must be attributed to the use of type-specific antiserum. The death of the patient in case 8 cannot be regarded as a failure of serum therapy, because the serum was administered late in the course of a fulminating illness.

SUMMARY

The recovery of the patients in 7 of 8 cases of H. influenzae meningitis can be attributed to the use of type specific serum.

University of Virginia Hospital.

Case Reports

SIMILAR UROGENITAL ANOMALIES IN IDENTICAL TWINS

JOHN KINGSLEY LATTIMER, M.D.
NEW YORK

A pair of twin boys with identical anomalies of the urogenital system was seen in the Babies Hospital service of the Squier Urological Clinic in New York. Each twin had glandular hypospadias, stricture of the meatus, dilatation of the urinary system and mild hypertension.

HISTORY AND EXAMINATION OF TWINS

TWIN "A."—On Nov. 3, 1942 a 10 year old Jewish boy was brought to the clinic because he had been

Fig. 1.—Photographs showing the glandular hypospadias and the meatal stricture of each twin. A bristle from a hand brush has been placed in the meatus of twin B (right).

having pain in the right side for three weeks. Since birth the child had been having urinary frequency and dribbling and had forced his urine out as a very fine spray. His urination was prolonged and often painful, and from time to time he had pains in the regions of both kidneys. His recent pains in the right flank had suggested renal infection on that side. The patient's only sibling was a twin brother who also had difficulty in voiding.

Physical Findings.—The patient was a husky white boy who did not appear to be ill. He had a normal temperature, but his blood pressure was 130 systolic and 80 diastolic. The kidneys were not palpable, but there was tenderness to deep pressure in the right flank. The inguinal rings were loose, and the testes would retract easily into the canals. Glandular hypospadias was present, with the urinary meatus situated at the margin of the coronal sulcus. There was such a tight stricture of the meatus that the latter would not admit a probe.

Laboratory Reports.—The urine was straw colored and cloudy, with a light sediment; its p_H was 7.5, and its specific gravity 1.018. A faint trace of albumin was present, but there was no sugar, acetone or occult blood (benzidine test). Microscopic examination of the urine, under high power, showed 10 to 25 leukocytes and 0 to 4 erythrocytes in each field with the white blood cells in clumps; amorphous phosphates were present. Culture of the urine gave a hemolytic strain of Staphylococcus albus. The ureteral urines from each side showed normal contents except for 2 to 10 white blood cells per high power field.

Examination of the blood showed nonprotein nitrogen 41 mg. per hundred cubic centimeters, hemoglobin 12.5 Gm. per hundred cubic centimeters, white cell count 14,200 (with polymorphonuclear leukocytes 77 per cent, lymphocytes 19 per cent and mononuclear leukocytes 4 per cent), and platelet and red cell counts normal. The Kline test gave a negative result, and the erythrocyte sedimentation rate was 40 mm. in one hour.

Roentgenograms.—A cystogram made after the introduction of sodium iodide revealed the capacity of the bladder to be 750 cc. The outline of the bladder was smooth, ovoid and large, but there was no reflux up the ureters. An intravenous pyelogram revealed that the renal pelves were distinctly dilated, although the minor calices were still sharply outlined. A retrograde pyelogram showed the presence of mild bilateral hydroureter. No valves were seen in the region of the neck of the bladder at cystoscopy.

Cystometrogram.—The wall of the bladder showed no tone until 500 cc. of fluid had been run in. At this point a normal muscular response began, and when 750 cc. had been introduced pain was felt and there was voiding around the catheter.

TWIN "B."—The twin brother had a similar history of straining on urination, a tiny urinary stream, frequency and dribbling, but without pain in the flanks.

Physical Findings.—The temperature was 99 F., and the blood pressure 126 systolic and 80 diastolic. The same glandular hypospadias was present, with a tight

Fig. 2.—Twin A (left) and twin B (right) shown writing with opposite hands.

meatal stricture. The meatus was so small that only a bristle from a hand brush would enter (fig. 1). The boy was completely normal in other respects. The close resemblance between the two boys left little doubt that they were identical, rather than homologous, twins (fig. 2). The similarity of their fingerprints and their opposite handedness were further evidences of this fact.

From the Babies Hospital Service of the Squier Urological Clinic.

Laboratory Reports.—The nonprotein nitrogen in the blood was 32 mg. per hundred cubic centimeters. The result of the Wassermann test was negative; the urine showed no pus, and the culture was sterile.

Roentgenograms.—A cystogram made after the introduction of sodium iodide showed a vesical capacity of 750 cc. and an outline which was so similar to that of the first twin that when the two roentgenograms were superimposed they appeared as one. In this boy, however, the dye refluxed up the left ureter, despite the fact that he had had no pains in the flanks (fig. 3). Cystoscopy revealed a relaxed left ureteral orifice but no valves in the urethra. Retrograde pyelograms showed the presence of mild bilateral hydronephrosis and of mild hydroureter on the left side.

Cystometrogram.—As in the other twin, there was no tone in the wall of the bladder until 500 cc. of fluid had been run in. A normal muscular response then began, and there was voiding around the catheter when 750 cc. had been introduced.

Fig. 3.—Cystograms (sodium iodide) for twin A (left), showing no reflux, and for twin B (right), showing reflux up the left ureter.

COURSE AFTER MEATOTOMY

A meatotomy was done on each of the boys. After the operations they both commented that they were able to void freely for the first time in their lives. Their blood pressures dropped within twenty days from 130 mm. systolic and 80 mm. diastolic to 110 mm. systolic and 60 mm. diastolic.

The dilated renal pelves slowly became smaller, but six months later the vesical capacities were both still over 500 cc. The ureteral reflux remained, but the urinary infection cleared. The degree of hypospadias was so slight that plastic procedures were considered inadvisable.

COMMENT

Strictures of the urinary meatus present a pediatric problem, and their danger is not always appreciated. Such strictures may be congenital, as were the ones just described, or they may follow infection around the meatus. A dilatation of the urinary tract results from the obstruction, and permanent renal damage may follow. Hypertension may or may not develop in the presence of renal back pressure.

It is of interest that in the 2 cases presented here the urinary back pressure on the kidneys appeared to cause a mild hypertension without causing an elevation of the nonprotein nitrogen. A parallel to this was noted in an analysis of the cases of the last 1,014 patients with prostatic urinary obstruction to undergo prostatectomy at the Squier Urological clinic; hypertension and elevation of the urea content of the blood were about equally common, but only rarely did they occur in the same patient. Of the 1,014 patients, 16 per cent had over 40 mg. of urea per hundred cubic centimeters of blood, and 14 per cent had a blood pressure above 180 systolic and 100 diastolic. Only 4 per cent of the patients had both hypertension and elevated blood urea.

A report on a pair of 10 year old twin boys with identical strictures of the urinary meatus has been presented. The same degree of dilatation of the bladder was present in each boy, with mild hydronephrosis and hypertension. After meatotomy the dilatation of the urinary tract decreased gradually, and the blood pressure fell to normal levels. These cases furnished an illustration of the fact that when a urogenital anomaly occurs in an identical twin one often sees the same anomaly reproduced in the other twin.

Presbyterian Hospital.

ARACHNODACTYLY IN FOUR SIBLINGS

WITH PNEUMOENCEPHALOGRAPHIC OBSERVATIONS OF TWO

HARRY D. PASACHOFF, M.D.; M. J. MADONICK, M.D., AND CARL DRAYER, M.D.
NEW YORK

Arachnodactyly was first described by Marfan,[1] in 1896, as observed in a 5½ year old girl who had abnormally long, slender fingers and toes. Achard[2] in 1902 described a second case of this disorder and selected the name arachnodactyly to indicate the "spider-like" appearance of the fingers and toes. This name was not well chosen, since it indicates only one of the many abnormalities present in this symptom complex. Although later authors suggested more comprehensive names, these have not been generally accepted, and the designation arachnodactyly, or Marfan's disease, persists. In addition to the long, slender bones of the hands and the feet, the complete syndrome is characterized by muscular atrophy, laxity of ligaments with their associated deformities and ocular and cardiac anomalies. The deformities which are commonly described are kyphosis, scoliosis, funnel chest, high position of the patella, hammer toes, pes planus and subluxation of joints. The commonest ocular anomaly is bilateral dislocation of the lenses associated with tremulous irises and is found in 62 per cent of the cases.[3] Other ocular abnormalities which have been observed are myopia, shallow anterior chamber, miosis and strabismus. Of the cardiac anomalies, patent interventricular septum and patent ductus arteriosus are the more common. Dolichocephaly, enlargement of the ears and a melancholy facial expression are other symptoms which have been noted.

Rados,[3] in a detailed review of the literature, recently tabulated a statistical survey of 204 cases of arachnodactyly which he was able to collect. In addition, he reported 10 cases of subluxation of the lens, in 7 of which there were unmistakable signs of arachnodactyly. In the 204 cases summarized, the patients were equally divided as to sex. One hundred and sixty-five patients (80.8 per cent) showed ocular changes, while 65 (31.8 per cent) displayed cardiac anomalies. Intelligence, as a rule, was particularly good. A hereditary background of this disease was definitely established in 59 cases (28.9 per cent), was questionable in 38 (18.8 per cent) and was absent or was not mentioned in 107 (52.5 per cent).

Recently we studied 2 siblings who showed many of the features of arachnodactyly. An opportunity was also afforded us to see the other 2 children in this family, and a note on their condition is included in this report. Our purpose in presenting this paper is, first, to supplement the number of case reports of this rare condition; second, to describe the results of air encephalography and intelligence studies in 2 cases, and, third, to record various features of the disease in 2 other siblings of this family.

REPORT OF CASES

CASE 1.—The first sibling, Lawrence, was born at term at the Morrisania City Hospital on Jan. 24, 1941. The mother's pregnancy was normal, and the delivery was normal and spontaneous. Soon after birth the infant was noted to have an abnormally shaped skull. The head was long and narrow, the frontal bones were flattened and the forehead bulged sharply, with a prominent ridge in the midline. Roentgen examination of the skull disclosed a flattening of the frontal bones. The width of the sutures, the density of the bone and the size were within normal limits. The child was discharged from the hospital on the tenth day.

The patient was not seen by us until July 27, 1942, when he was readmitted to the hospital for observation prior to his placement in an institution. Physical examination revealed a boy 18 months old, 35 inches (88 cm.) tall, normal height of a boy of his age being 32 inches (81 cm.), pale and peculiar in appearance. His head had retained the abnormal contour observed at birth. The forehead was pointed, with a sharp ridge in the midline, and the back of the head was flat, with occipital bosses. The anterior fontanel was closed. His ears were large, though normal in shape. The eyes were closely set, the facies was dull and his expression was melancholy (fig. 1). The teeth were normal and closely set. The chest was deeply funnel shaped, and there was considerable kyphosis in the lumbar region. The extremities were normal in length, but the fingers and the toes were exceptionally long. Except for a soft systolic nontransmitted murmur to the left of the sternum, no abnormalities could be detected in the child's heart. A striking feature was

From the Pediatric Service of the Morrisania City Hospital, Dr. Louis H. Barenberg, director.

1. Marfan, A. B.: Un cas de déformation congénitale des quartre membres plus prouncée aux extrémités characterisée par l'allongement des os avec un certain degré d'amincissement, Bull. et mém. Soc. méd. d. hôp. de Paris **13**:220, 1896.

2. Achard, C.: Arachnodactylie, Bull. et mém. Soc. méd. d. hôp. de Paris **19**:834, 1902.

3. Rados, A.: Marfan's Syndrome (Arachnodactyly Coupled with Dislocation of the Lens), Arch. Ophth. **27**:477 (March) 1942.

the laxness of the muscles and the ligaments, enabling hypermobility of the joints, with unusual hyperextensibility of the hands and the feet. Careful examination of the eyes revealed them to be normal; no ectopia lentis, iridodonesis or myopia was observed. Neurologic examination showed no abnormalities.

Investigation of the child's mental status revealed that he played with toys and enjoyed them. He sat well but could not stand unsupported, although his inability to stand might have been due to his physical defects. He showed some comprehension, attempted to feed himself and could say several words. Attempts to determine his intelligence were unsatisfactory because of his age, but an estimate arrived at by using the Kuhlman-Binet test showed the child to be retarded, with a mental age of 13.2 months.

Urinalyses repeatedly gave negative results. The hemoglobin content of the blood was 87 per cent, the erythrocyte count 4,650,000 and the leukocyte count 6,250, with 72 per cent polymorphonuclear leukocytes, 27 per cent lymphocytes and 1 per cent monocytes. The blood contained 11.3 mg. of calcium and 4.7 mg. of phosphorus per hundred cubic centimeters. The Wassermann reaction of the blood was negative. The spinal fluid was clear and was not under pressure. The spinal fluid contained 85 mg. of sugar, 21 mg. of protein and 743 mg. of chlorides per hundred cubic centimeters. There were no cells, and the results of the Wassermann and the colloidal gold test were both negative. Roentgen examination of the limbs showed no abnormality in the structure of the bones. Roentgen examination of the skull revealed a narrow anteroposterior diameter, while the vertical diameter was longer than normal. There was no evidence of disease of the bones. Air encephalography was done. Eighty cubic centimeters of fluid was removed and replaced with air. Roentgenograms taken after the injection of air showed moderate dilatation of the lateral ventricles of the brain, the outlines of which were smooth and symmetric, with no displacement (fig. 2).

Fig. 1.—Photograph showing patient 1 at the age of 18 months. Note the ridge in the forehead, large ears, melancholy expression, funnel-shaped chest and kyphosis.

CASE 2.—The other sibling, Gertrude L., according to her mother's statement, was delivered normally at term. At the time of her admission to the hospital, she was 2½ years old, appeared pale and dull and had a stare, a symptom often observed in patients with high grade myopia (fig. 3). She was 37 inches (93 cm.) tall (the normal height of a girl 2½ years old being 35 inches [88 cm.]). Her fingers and toes were longer than normal. There were moderate pes planus and genu valgum. She showed muscular atony and laxness of ligaments. Examination of the eyes revealed bilateral iridodonesis. Both lenses were partially dislocated, the right upward and the left upward and outward. The pupils reacted to light and dilated with atropine. Vision was limited to objects held at close range. The ears were of normal shape and size. Neurologic examination revealed no abnormalities.

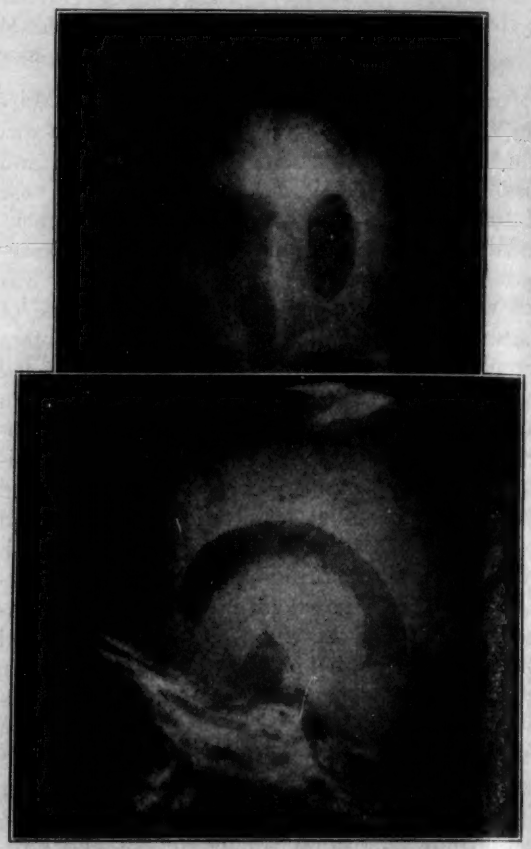

Fig. 2 (case 1).—Encephalograms taken after injection of air, showing moderate dilatation of the lateral ventricles.

The history indicated retarded development. The child did not sit until she was 12 months of age. She walked at the age of 19 months. In the ward she prattled continuously and made squeaking sounds but uttered nothing intelligible. Mental investigation showed her to be uncooperative, inattentive and unable to follow instructions. Her mental age, as determined by the Kuhlman-Binet test, was approximately 16.5 months, and she was classified as a moron.

Urinalysis gave normal results. The hemoglobin content of the blood was 90 per cent, the erythrocyte count

4,850,000 and the leukocyte count 8,720, with polymorphonuclear leukocytes 70 per cent, lymphocytes 28 per cent and monocytes 2 per cent. The blood contained 10.7 mg. of calcium and 2.1 mg. of phosphorus per hundred cubic centimeters. The Wassermann reaction of the blood was negative. The spinal fluid was clear and was not under pressure. It contained 65 mg. of sugar, 20 mg. of protein and 750 mg. of chlorides per hundred cubic centimeters. There were no cells, and the Wassermann and the colloidal gold tests both gave negative reactions. Roentgen examinations showed the skull and the limbs to be normal. Seventy-five cubic centimeters of spinal fluid was removed and replaced with air. Roentgen examination showed the ventricles of the brain to be normal in position and contour, but they appeared slightly dilated in the lateral view (fig. 4).

Observations on Other Members of Family.—During hospitalization of these 2 children we obtained some information concerning the other members of the family. The father was not observed, but the mother reported him to be 6 feet (182 cm.) tall and to have long extremities, with exceptionally long fingers and toes. He wears size 12-2A shoes. The paternal grandfather was of similar stature and had considerable difficulty with his eyes, wearing extremely thick lenses. The mother, whom we saw, was tall and slender, with long fingers and toes, which were not inconsistent with her general build. She had no ocular anomalies.

Two other children in the family were examined by us. Valerie L., aged 4 years, was 48 inches (121 cm.) tall (normal height of a girl 4 years old being 39 inches [99 cm.]). She had been admitted previously to this hospital in the ophthalmologic service for discission of a cataract. We noted a well developed child, with a happy disposition and of average intelligence. Her fingers and toes wefe long; there were bilateral pes planus and some hyperextension at the wrists. Her eyes showed bilateral iridodonesis and narrow anterior chambers. Both lenses were dislocated upward and inward, and the right lens had a cataract.

Fig. 3.—Photograph showing patient 2, aged 30 months, at the left and patient 1 at the right. Note dull expression, long fingers and toes and genu valgum of patient 2.

George L., aged 5½ years, was 50 inches (127 cm.) tall (normal height of a boy of his age being 44 inches [111 cm.]). He appeared well developed but had a melancholy expression. He, too, showed bilateral iridodonesis with no dislocation of the lenses. His fingers and toes were also long.

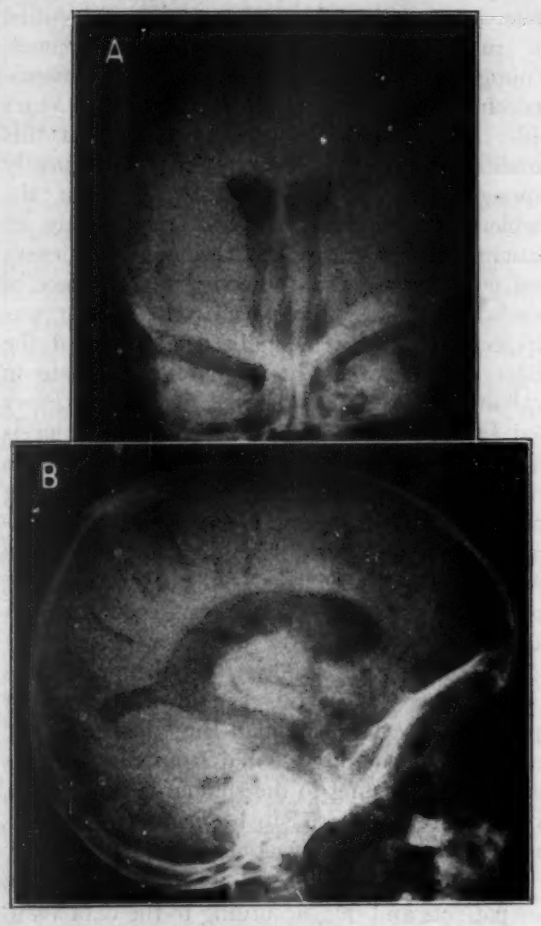

Fig. 4 (case 2).—*A*, Encephalogram showing the ventricles normal in position and contour. *B*, Encephalogram showing the ventricles slightly dilated.

None of the children had cardiac anomalies.

COMMENT

Four siblings have been described, each showing features of Marfan's disease. Lawrence (case 1) presents a characteristic picture, with the exception of the ocular changes. This may be explained on the basis that arachnodactyly is a hereditary disease which is transmitted by changes in a varying number of chromosomes. If only chromosomes concerned with mesodermal development are involved, the ocular symptoms are absent. If chromosomes concerned with ectodermal development are also affected, the complete syndrome will be present.

Rados [3] and Baer [4] maintained that intelligence as a rule is particularly good. Pino, Cooper and Van Wien [5] wrote that mentality is generally normal. However, in their case 1, a boy of 6 years was obviously mentally defective and after a psychologic examination was classified as suffering from cerebral maldevelopment. Young [6] reported 2 cases in which the patients' speech was unintelligible until they were 3 years old. Lloyd [7] went so far as to say that this condition has been observed more frequently among young inmates of institutions for the feebleminded. However, this refers only to patients with bilateral dislocation of the lenses and not to those with the complete syndrome of arachnodactyly. In his case 2 the patient was suspected of being mentally defective, and the sister of the patient in his case 5 was late in walking and had had delayed dentition. Piper and Irvine-Jones [8] stated that the mental levels of their patients ranged from slight backwardness to exceptional intelligence, most of them being mentally normal. Rambar and Denenholz [9] expressed the opinion that their patient, 26 months old, was mentally retarded, but they were unable to give the child psychologic tests because of his lack of cooperation. We investigated the intelligence of 2 of the children, but the procedures used for persons of this age level are at best approximate. The Kuhlman-Binet test employed relies on information elicited from the patient's mother. According to the standards in this test, both children appeared to be mentally retarded, and 1 (Gertrude L.) was classified as a moron.

Air encephalography was performed on 2 of our patients and this, according to the data available to us, was the first time that this procedure had been done in such a case. Eighty and 75 cc. of spinal fluid were withdrawn, respectively. The fluid drained freely, and considerably more could have been removed in each case. In 1 of the children an internal hydrocephalus was noted, while in the other child the ventricles appeared to be somewhat dilated on lateral view. The presence of hydrocephalus was mentioned in the autopsy reports of Börger,[10] Piper and Irvine-Jones [8] and Rambar and Denenholz.[9] Börger [10] found a considerable increase of fluid in the subarachnoid and subdural spaces. The brain in the case of Piper and Irvine-Jones [8] showed slight internal and external hydrocephalus, involving especially the posterior horn of the lateral ventricles. Rambar and Denenholz [9] found that the lateral ventricle was dilated and the leptomeninges were separated by an increased amount of fluid. Thus there was noticeable dilatation of the ventricular system in 3 of the 5 patients given postmortem examinations.

We are able to add to the series by means of encephalography 1 more definite case of internal hydrocephalus and also a case in which there was some evidence of dilatation of the ventricular system on lateral view. The presence of hydrocephalus and mental retardation indicates that the ectoderm is involved in addition to the more pronounced and more emphasized mesodermal changes.

SUMMARY

Cases of 4 siblings showing characteristics of Marfan's disease are reported. Two of the children were observed during a stay in the hospital. They showed mental retardation, one being classified as a moron. Air encephalography revealed definite internal hydrocephalus in one and some dilatation of the ventricular system in the other. Information concerning the hereditary background indicated that the father and the paternal grandfather had elements of this disease and that its transmission was through them.

910 Grand Concourse.

4. Baer, R. W., in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1942, vol. 4, chap. 26.

5. Pino, R. H.; Cooper, E. L., and Van Wien, S.: Arachnodactyly and Status Dysraphicus: A Review, Ann. Int. Med. **10**:1130, 1937.

6. Young, M. L.: Arachnodactyly, Arch. Dis. Childhood **4**:190, 1929.

7. Lloyd, R. I.: A Second Group of Cases of Arachnodactyly, Arch. Ophth. **17**:66 (Jan.) 1937.

8. Piper, R. K., and Irvine-Jones, E.: Arachnodactylia and Its Association with Congenital Heart Disease, Am. J. Dis. Child. **31**:832 (June) 1926.

9. Rambar, A. C., and Denenholz, E. J.: Arachnodactyly: Report of a Case with Autopsy, Including Histologic Examination of Eye, J. Pediat. **15**:844, 1939.

10. Börger, F.: Ueber zwei Fälle von Arachnodactylie, Ztschr. f. Kinderh. **12**:161, 1914.

Progress in Pediatrics

MENTAL DEVELOPMENT OF CONGENITALLY HYPOTHYROID CHILDREN

ITS RELATIONSHIP TO PHYSICAL DEVELOPMENT AND ADEQUACY OF TREATMENT

HILDE BRUCH, M.D.,* AND DONOVAN J. McCUNE, M.D.
NEW YORK

The purpose of this paper is to examine the mental development of children with congenital hypothyroidism. There are few developmental disorders which show such striking somatic response to treatment; the literature abounds with reports and illustrations of the miraculous changes which have taken place in retarded, misshapen children after administration of an adequate amount of thyroid. Details of physical progress are usually described accurately; references to mental development are commonly vague. Even the most enthusiastic reports convey some uneasiness about the ultimate mental capacity of these children.

Only a few authors [1] have attempted to evaluate as objectively and quantitatively as possible the relationship of mental development to physical progress. The reports of these few contain data which point to a certain lack of dependence of mental development on the adequacy of treatment and the degree of restoration of the physical state. However, the great majority of reports —only a few of which have been included in this survey—and, even more, the prevailing clinical opinion express the view that inadequate mental development might have been prevented had treatment been instituted earlier or carried out more intensively. Good results in the intellectual sphere are attributed to adequacy of treatment. The concept that mental development is favorably influenced by thyroid medication is so widespread that it is common practice to give large amounts of thyroid to children whose mental development is clearly not of hypothyroid origin in the hope of augmenting intellectual capacity. The object of this paper is to appraise the correctness of the foregoing concepts.

HISTORICAL ASPECTS AND REVIEW OF THE LITERATURE

The condition with which we are concerned is properly known as congenital hypothyroidism. It is frequently referred to as cretinism. This is not entirely correct usage, since the latter term properly designates endemic congenital hypothyroidism, a disorder which does not respond to thyroid therapy. However, since cretinism is a short and convenient name it will be used here as synonymous with the sporadic variety of hypothyroidism. The distinction between the two species was first made by the Englishman Fagge [2] in 1871. He recorded the sporadic occurrence of a developmental peculiarity closely resembling endemic cretinism, which had been identified earlier. Fagge related the disorder to atrophy of the thyroid gland. Gull,[3] referring to Fagge's earlier report, recognized the existence of sporadic cretinism in adults and emphasized the presence of thyroid disturbances in these cases. Gull described the cretinoid condition in the child as "characterized by a broad, flat nose, and thick lips; broad hands and feet; and the mild tranquil disposition so different from the mischevious tendencies of the idiot with whom these children are so generally associated." He described how in one of the adults "the mind which had previously been active and inquisitive had assumed a general, persistent indifference corresponding to the muscular languor; but the intellect was unim-

From the Departments of Psychiatry and Pediatrics, College of Physicians and Surgeons, Columbia University, and the Babies Hospital.

* Aided by a grant from the Josiah Macy, Jr. Foundation.

The psychometric examinations were performed by Dr. Z. Piotrowski, of the New York Psychiatric Institute, and by Miss Gladys Tallman, of the New York Neurological Institute.

1. (*a*) Gesell, A.; Amatruda, C. S., and Culotta, C. S.: Effect of Thyroid Therapy on the Mental and Physical Growth of Cretinous Infants, Am. J. Dis. Child. **52**:1117 (Nov.) 1936. (*b*) Lewis, A.: A Study of Cretinism in London, with Especial Reference to Mental Development and Problems of Growth, Lancet **1**:1505, 1937; **2**:5, 1937. (*c*) Goodkind, R. P., and Higgins, H. L.: Hypothyroidism in Infants and Children with Reference to the Ultimate Prognosis Concerning Intelligence and to the Withdrawal of Thyroid Therapy as a Diagnostic Measure, New England J. Med. **224**:722, 1941.

2. Fagge, C. H.: On Sporadic Cretinism Occurring in England, Med.-Chir. Tr. **54**:155, 1871.

3. Gull, W. W.: On a Cretinoid State Supervening in Adult Life in Women, Tr. Clin. Soc. London **7**:180, 1874.

paired. Although there were deposits of fat, fatness did not comprehend the pathology." Concerning other cases he stated that the intellect was not materially impaired but that the nervous power on the whole was lessened and hence the changes in temperament had arisen. The name myxedema, which later came into use for sporadic cretinism, was coined in 1883 by a committee for the study of this disorder.

A report on myxedema in 1888 contained a summary of 109 cases.[4] The literature was subsequently enlarged by numerous reports illustrating the brilliant success of thyroid treatment. The writers of critical reviews of the period were not always able to confirm these optimistic claims. Concerning the mental development of cretins Siegert[5] wrote in 1910 that the intellectual retardation corresponded to the inhibition and degeneration of physical development; further, that in his cases the mental impoverishment ranged from mild deficiency to total idiocy. He found that in response to treatment the intellectual development might follow the same accelerated tempo as the physical improvement, but he also reported that in many cases mental growth lagged behind physical progress in spite of long-continued and energetic glandular therapy. In other cases mental progress was more satisfactory and only mild retardation reminded one of the former defective state. Wieland[6] in 1912 centered his discussion mainly on the question whether hypothyroidism in the child was congenital or acquired. He considered acquired hypothyroidism to be exceedingly rare and expressed the opinion that probably in most cases of hypothyroidism there was a primary malformation of the thyroid gland even though the clinical features were not manifest at the time of birth. He also found that the therapeutic results showed great variation from case to case and that the psychic function frequently remained uninfluenced.

The tone of many publications during the next two decades is more encouraging than that of the foregoing reviews. In 1924 Lazar and Nobel[7] reported longitudinal observations on hypothyroid children whose mental development they had measured. They came to the conclusion that the quantitative differences of intellectual development stood in direct relationship to the time of beginning of treatment and to its regularity. They found certain similarities in the intellectual development: "All show their abilities best where the quick perception of sensory impressions is involved and where, in the course of life and learning, mechanization becomes possible. On the other hand, they fail in all intellectual achievement which makes demands on the thinking ability over a long period of time. In addition a specific deficiency of speech development is apparent. The hypothyroid children remain retarded with regard to speech understanding much more than mongoloid children." This report is based on observations of 6 children. None of these patients had been treated adequately or continuously, and all showed signs of retardation in physical development. In some cases treatment had been interrupted for five to seven years during the first World War, since it was impossible to obtain the necessary amounts of thyroid. The factor of inadequate treatment makes the conclusions of these authors of limited significance. Hochsinger[8] and Kerley[9] reported that in prolonged observations of hypothyroid children in private practice they found rather favorable results in both physical and mental development.

The reports of observers of larger groups of patients in hospitals and clinics are less encouraging. Impressed by the frequency of mental retardation, Aldrich,[10] in a review in 1936, advocated administration of the largest tolerable dose of thyroid. He expressed the hypothesis that a dose which is merely competent to foster physical growth might be insufficient for the "development of structures which one cannot observe directly but which may be of determining significance in the ultimate competency of the child." He told of seeing congenitally hypothyroid children who had progressed through the grade schools without arousing suspicion of developmental difficulties, then went on to say that "it would seem reasonable to suppose that such individuals if continuously treated might mature through adolescence to average adult

4. Gull, W. W.: Report of a Committee of the Society Nominated December 14, 1883, to Investigate the Subject of Myxedema, Tr. Clin. Soc. London **21**: 298, 1888.

5. Siegert, F.: Myxoedem im Kindesalter, Ergebn. d. inn. Med. u. Kinderh. **6**:601, 1910.

6. Wieland, E.: Ueber hypothyreotische Konstitution und über frühzeitig erworbene Athyroeose, Ztschr. f. Kinderh. **4**:310, 1912.

7. Lazar, E., and Nobel, E.: Beitrag zur Prognose des kindlichen Myxoedems, Ztschr. f. Kinderh. **38**:235, 1924.

8. Hochsinger, C.: Ein Fall der wegen einer kongenitalen Athyreose seit seinem 13. Lebensmonate mit Schilddrüsenpräparaten erfolgreich behandelt wird, Wien. med. Wchnschr. **76**:316, 1926.

9. Kerley, C. G.: End Results in the Cretin, Arch. Pediat. **57**:432, 1940.

10. Aldrich, C. A.: Growth and Development: The Endocrine Glands and Growth; the Thyroid, J. Pediat. **8**:381, 1936.

competency." Wilkins [11] demonstrated that the careful evaluation of the rate of growth and of osseous and mental development might serve as a guide to thyroid treatment. He suggested the possibility that some cretins attained normal physical development but remained permanently mentally retarded because of delay in the beginning of treatment, use of inadequate amounts of thyroid or interruption of treatment. He also pointed out the possibility that in some instances irreparable damage to the nervous system had occurred during intrauterine life or early infancy. He found that as a rule the earlier intensive treatment was begun the better the final result. Brown, Bronstein and Kraines [12] applied psychologic tests to 29 cretins and 4 children with juvenile hypothyroidism over a period of one to seven years. They found evidence that early recognition of the abnormal condition and vigorous and persistent treatment are the important factors in producing good mental development. They also found that the mental development progressed at approximately the same general rate as in the average child, only at a lower level. In another study [13] of the social adjustment of children with thyroid deficiency the same authors emphasized that adequate treatment even in the presence of low intelligence helped the child to become better adjusted and to be better accepted within the family group and among his playmates. However, thyroid therapy did not overcome low intelligence or an unwholesome parental attitude; moreover, physical improvement of the child was not always followed by improvement of parental attitude.

Gesell [1a] and his co-workers assembled data on 6 cases of hypothyrodism in which the condition was recognized and adequately treated in infancy. These children were observed for periods of fourteen months to ten years and were studied in the Clinic of Child Development of Yale University. It is one of the cardinal doctrines of the Gesell school that there is a fundamental unity between physical and mental expressions of growth. The close correlation between these two aspects of development is demonstrated by extensive longitudinal observations on normal infants and children. In hypothyroid children, however, while rapid improvement of physical maturation took place, the mental development attained varied widely and ranged from normal intelligence to severe deficiency. The report of Gesell and his co-workers emphasizes that each cretin has a distinctive optimal response and that the ultimate outcome can be forecast by careful appraisal of the changes in growth and behavior during the initial months of treatment.

The discrepancy between success in promoting physical development and great variability in mental achievement is also brought out in a large scale study by Lewis, [1b] who made a survey of 79 cases of cretinism. He observed patients from the clinics of several London hospitals and from institutions for persons with mental deficiency. The ages of the patients ranged from 3 to 58 years. In many instances the diagnosis had to be made from the history and from old records. The authors were unable to correlate the amount of treatment with the persistence of physical peculiarities. In evaluating intelligence they emphasized that slowness of response to verbal direction may create the impression of greater deficiency than is actually the case. Mental development showed wide variation, with intelligence quotients ranging from 10 to 120. Four of these patients had quotients above 100; 12 rated between 80 and 100. However, the proportion of defectives in the entire study was high. The value of this observation must, of course, be viewed in the light of the relatively unproved character of the diagnosis. An effort was made to assess the final result in relation to the age of onset and to the interval before treatment was begun. This could not be accomplished with precision; the conclusions were therefore drawn with some reserve. The majority of those whose intelligence quotients were above 70 had received fairly adequate treatment; however, early and adequate therapy by no means supplied insurance against gross mental defect. The authors found only crude correlation between adequacy of treatment and the intellectual level finally attained. The shortcoming of this paper is the unreliability of the information on early diagnosis and treatment, but the formulation of the problem and the approach to a solution are stimulating. Goodkind and Higgins [1c] reported in 1941 on 26 patients who had been under sustained treatment for five and a half to twenty-four years. The intelligence quotients ranged from 15 to 112, with a mean of 72. Twelve patients were unusually small in stature; their mean intelligence quotient was 68. "Although the men-

11. (*a*) Wilkins, L.: The Rates of Growth, Osseous Development, and Mental Development in Cretins as a Guide to Thyroid Treatment, J. Pediat. **12**:429, 1938. (*b*) Wilkins, L., and Fleischmann, W.: The Diagnosis of Hypothyroidism in Children, J. A. M. A. **116**:2459 (May 31) 1941.

12. Brown, A. W.; Bronstein, I. P., and Kraines, R.: Hypothyroidism and Cretinism in Childhood: VI. Influence of Thyroid Therapy on Mental Growth, Am. J. Dis. Child. **57**:517 (March), 1939.

13. McDonald, J. W.; Brown, A. W., and Bronstein, I. P.: Background and Social Adjustment of Thyroid-Deficient Children Receiving Glandular Therapy, Am. J. Dis. Child. **59**:1227 (June) 1940.

tal level tended to be higher in patients of normal height, in several cases of normal mentality the physical response to glandular therapy was subnormal. . . . The age at which diagnosis was made and treatment started was by no means the deciding factor in the ultimate mental capacity. . . . The mental retardation may quite well have the same etiologic cause as the athyria in certain cases; and the athyria may not be the cause of the mental retardation."

Although the association of mental deficiency and thyroid deficiency was early recognized, pathologic studies of the brain have not been reported frequently. The records of the Babies Hospital in New York contain 3 reports of autopsies on children with congenital hypothyroidism. The brain of 1 child was not examined. In the brains of the other 2 no gross lesion was observed. In 1910 Siegert [5] summarized the earlier literature in the general statement that there were no characteristic anatomic changes in the brain except simple developmental disturbances such as are found in other forms of idiocy. Isenschmid,[14] however, emphasized that the failure of the earlier investigators to find such changes might result merely from inadequate technic of investigation. He observed in experiments with cats that thyroidectomy was followed by some changes in practically all cells of the central nervous system. In a more recent review of the literature Wegelin [15] concluded that the anatomic foundation of the mental defects in cretinism remains practically uninvestigated. The clinical literature also fails to record direct investigations of the brain by such methods as pneumoencephalography and electroencephalography.

It is hoped that this cursory review illustrates the character and extent of the prevailing uncertainty concerning the mental development of the congenitally hypothyroid child and supplies justification for the report of new observations which bear on the matter.

PERSONAL OBSERVATIONS

The report which follows is based on longitudinal studies of 23 children (7 boys and 16 girls) who are or have been patients at the pediatric division of Vanderbilt Clinic, the outpatient department of the Babies Hospital in New York. These children were selected from a much larger group because their records contained sufficient information to permit a planned appraisal. Cases in which there was the slightest doubt of the diagnosis have not been included.

The picture of cretinism in childhood has been described and illustrated so frequently that we refrain from reviewing the symptoms here. In no case was there reason to assume that the disorder was not congenital. We have considered the diagnosis as definite only when adequate treatment was followed by disappearance of the features typical of hypothyroidism and their replacement by a more normal aspect. In addition, treatment was interrupted for short periods as a diagnostic test: In cases of true hypothyroidism some of the symptoms will reappear and characteristic and measurable metabolic changes will develop.

Numerous laboratory examinations were carried out, but only those which proved particularly helpful in evaluating the degree of thyroid deficiency and the progress of treatment will be mentioned. Skeletal age, estimated from roentgenograms of the knee, wrist, elbow or other regions, was determined repeatedly for all patients. Delay in skeletal maturation was present in all cases before treatment. In a few instances previous treatment had been insufficient and had left retardation uncorrected. Before the onset of puberty progress in skeletal maturation is probably the most reliable index of the adequacy of treatment. Acceleration of statural growth in response to treatment also occurs with great regularity, but if the beginning of treatment is much delayed the final height may remain below normal.

Fluctuations of the levels of serum cholesterol and of urinary creatine have been widely studied during the past decade as aids in diagnosis and treatment. We have found both examinations helpful for determining adequate dosage of thyroid; this is particularly true of the serum cholesterol, since specimens can be collected at the time of an office visit. Single estimations may be misleading because the concentration of cholesterol in the serum of young untreated cretins commonly falls within the normal range. During the continuation of adequate treatment a characteristic level can be found for each patient. Noticeable deviations from this level usually call for readjustment of the dose of thyroid. These observations are particularly helpful at the time of puberty, when measurement of skeletal age ceases to supply adequate information.

It will be noted that we do not include the determination of basal metabolism among the helpful laboratory tests. Accurate values are

14. Isenschmid, R.: Histologische Veränderungen im Zentral-Nervensystem bei Schilddrüsenmangel, Frankfurt. Ztschr. f. Path. **21**:321, 1918.

15. Wegelin, C.: Schilddrüse. 31. Athyreose und Hypothyreose. Nervensystem, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1926, vol. 8, p. 351.

not easily obtained for young cretins, many of whom are mentally retarded. Furthermore, considerable uncertainty attends the evaluation of results in view of the great variation of body build in relation to age.

Turning now to a description of our case material, the pertinent data will be found in the table. The cases are arranged according to the result of the last psychometric examination (column 8), which was made when the child was of the age stated in column 4. The height quotients (column 6) and the appraisals of skeletal age (column 7) are derived from observations made at the same time as the psychometric examinations. In most instances several mental tests were given. The figures for intelligence quotients in the table refer to the result of the Stanford-Binet test except for extremely young or much retarded children. The observations extend over a period of several years; hence two modifications of this test were used, forms L and M. The differences in results of the modified tests were neglected in our computations, since the changes which are significant to our inquiry fall outside the discrepancies between the two forms of the test. The Pintner-Patterson performance test, the Goodenough drawing scale, the Terman vocabulary test, the Kuhlmann-Binet test and the Merrill-Palmer scale were also used, although not all tests were given in every instance. The results of different tests are mentioned in the individual reports only if these results were significantly discrepant.

Height is recorded as "height quotient." This was calculated in the same way as the intelligence quotient, namely $\frac{\text{Height age}}{\text{Chronologic age}} \times 100$. The fiftieth percentile of the Burgess growth chart [16] was taken as the basis for the calculation of height age. Skeletal age (column 7) was determined from roentgenograms of the wrist and knee according to the standards of Todd.[17] Close agreement with these standards was called "normal" and is indicated in the table as N (11 cases). Deviations of about six months are designated as N + (2 cases) or N — (5 cases). Delay in ossification of more than six months, sometimes of several years, was called retarded (R) (5 cases).

The age at which treatment was started is recorded in column 5. In 13 cases treatment was begun before the age of 1 year. The earliest age was 3 months (case 17). Four children were between 1 and 3 years of age, and 6 were more than 3 years old. The latest age at which treatment was started was 8 years and 2 months, case 22. In this case as well as in case 2 the patient may have had some thyroid treatment before she was seen in our clinic, but the amount of thyroid was certainly inadequate and it was given for only a short time if at all. As far as we know, in the other cases in which treatment was started at a later age there had been no previous treatment.

The last two columns deal with the rating of treatment as to adequacy and regularity. We have called the dose adequate if it was large enough to bring the retarded physical development to normal and then to permit progress at

Summary of Developmental Data Relating to Twenty-Three Cases of Congenital Hypothyroidism

(1)	(2)	(3)	(4)		(5)		(6)	(7)	(8)	(9)	(10)
			Present Age		Age When Treatment Started					Rating of Treatment	
Case No.	Initials of Patient	Sex	Yr.	Mo.	Yr.	Mo.	Height Quotient	Skeletal Age	Intelligence Quotient	Adequacy	Regularity
1*	P. L.	F	3	11	0	6	125	N+	109	Adequate	Regular
2*	R. P.	F	16	4	5	5	75	R	96	Adequate	Irregular
3	R. E.	M	9	9	0	11	104	N	91	Adequate	Regular
4*	W. S.	M	4	8	0	8	114	N—	80	Adequate	Regular
5	L. B.	F	7	8	0	4	97	N+	78	Adequate	Regular
6	E. S.	F	9	8	0	5	107	N	72	Adequate	Regular
7	Sh. K.	F	17	3	4	..	N+	N	71	Adequate	Regular
8	S. Z.	F	2	5	0	5	80	N	69	Adequate	Irregular
9	E. N.	F	7	7	0	6	67	R	68	Inadequate	Irregular
10	L. C.	F	10	0	3	7	81	N	68	Adequate	Regular
11	T. K.	F	6	4	1	1	121	N	67	Adequate	Regular
12	J. L.	F	11	3	2	1	97	N—	64	Adequate	Regular
13*	M. B.	M	10	1	2	8	85	N	62	Adequate	Regular
14	J. G.	F	3	0	0	10	65	N—	55	Adequate	Irregular
15	E. B.	M	11	1	1	0	107	N—	54	Adequate	Regular
16	L. B.	M	12	7	3	1	88	N	53	Adequate	Irregular
17	J. D.	M	2	1	0	3	67	R	53	Adequate	Irregular
18	J. C.	M	14	8	0	6	90	N—	50	Adequate	Regular
19	J. F.	F	12	3	2	0	101	N	44	Adequate	Regular
20	P. R.	F	16	0	5	2	79	N	44	Adequate	Regular
21	T. Ka.	F	11	6	1	0	58	R	34	Inadequate	Irregular
22*	S. C.	F	13	10	8	2	82	R	28	Adequate	Regular
23*	E. L.	F	6	3	0	9	117	N	21	Adequate	Regular

* Cases reported in detail.

16. Burgess, M. A.: Construction of Two Height Charts, J. Am. Stat. A. **32**:290, 1937.

17. Todd, T. W., and others: Atlas of Skeletal Maturation, St. Louis, C. V. Mosby Company, 1937.

a normal rate. Most children remained under continued supervision of the clinic. Only 2 patients were regarded to have been inadequately treated, and in both cases the mother had administered less thyroid than had been prescribed. These 2 patients returned for examination at highly irregular intervals. Treatment was rated "regular" when there were no interruptions of treatment except for the deliberate brief withdrawal of thyroid for the purpose of verifying the diagnosis or making special investigations during the hypothyroid state. In 7 cases treatment was interrupted by the parents, and the children went unsupervised for variable periods. In the individual cases the duration of treatment can be calculated by subtracting the age at which treatment was started (column 5) from the age at the time of tabulation (column 4). It ranges from 1 year and 10 months to 14 years and 2 months. Many of the children have been observed beyond this period.[18]

The table contains the result of only the latest psychometric examination of each child. In most instances several tests were made over a period of years. The first was not carried out until a considerable time, sometimes years, after the start of treatment. The changes in individual cases are illustrated graphically in figures 1 and 2. In these charts the chronologic age is plotted on the abscissa and the mental age on the ordinate. The developmental charts for the 6 patients whose cases are reported in detail are constructed similarly. The line extending at 45 degrees indicates equality between mental age and chronologic age. In the psychometric literature this is generally referred to as intelligence quotient 100. This 45 degree line represents the expected rate of progress for children with a normal intelligence quotient. If one wishes to evaluate the progress of children with subnormal mental development it is necessary to draw auxiliary lines indicating the expected rate of progress for various levels of intelligence. Let us assume the case of a defective child with a relative mental age of 0.5 years. This child would have a mental age of 2 at the age of 4 years, of 3 at the age of 6, of 4 at the age of 8 and so on. All determinations would fall on the auxiliary line designated 50. One could say that this line represents the expected rate of progress for a child of this mental level. The auxiliary lines designated 90, 75 and 25 were constructed in like manner. These lines are helpful in evaluating the effect of treatment. If there is acceleration of development the curves which connect different examinations for the same person will tend to cross the auxiliary lines and to rise toward the 45 degree line or even to cross it. This is demonstrated most clearly by the curves for statural growth and skeletal maturation in the individual developmental charts. If there is retardation or arrest of development the curves will tend to approach an auxiliary line representing a lower level or to approach the horizontal.

The mental development of hypothyroid children shows two distinct patterns of progress. In most instances the curves representing individual development follow fairly closely the lines of expected progress. In other instances, mostly involving children of low mentality, there is a distinct decline in intelligence quotient which is represented on the charts by progress lines running more or less horizontally instead of at the slope of expected progress.

There was only 1 patient (R. E. in figure 1; case 3 in the table) whose intelligence quotient increased conspicuously. This boy had been under treatment since the age of 11 months. At the time of the first test he was 5 years and 5 months of age and had a mental age of 4 years (intelligence quotient, 74). He had a severe speech defect which may have accounted for the low result. On three later examinations, when he was 7 years, 8 years and 9 years, 9 months of age, his intelligence quotient was approximately 90.

An apparent decline in intelligence quotient represents arrest of mental development at a low level. In evaluating these figures it must be borne in mind that in all cases the first formal psychometric examination was carried out many months, sometimes years, after treatment had been started. Data concerning initial changes in the relative mental level are therefore not available. All of our records contain numerous descriptions of improvement in alertness, adaptability and responsiveness after the beginning of treatment, which will be mentioned in the reports on individual cases.

The correlation between the figures for mental and somatic development is low. The coefficient of correlation for height quotient (column 6) and intelligence quotient (column 8) is only 0.309. (Case 7, in which the height at the time of the computation fell outside the fiftieth percentile of the Burgess chart, has not been included in this evaluation.) The mean height quotient for all the children is 92.4; that is, the stature of the treated hypothyroid child approaches normal. The mean intelligence quotient is only 62.2, a value indicating significant mental retardation. If the results of examinations are grouped according to the ages of the patients at the begin-

18. All figures were computed in 1941, before one of us (H. B.) went on a leave of absence.

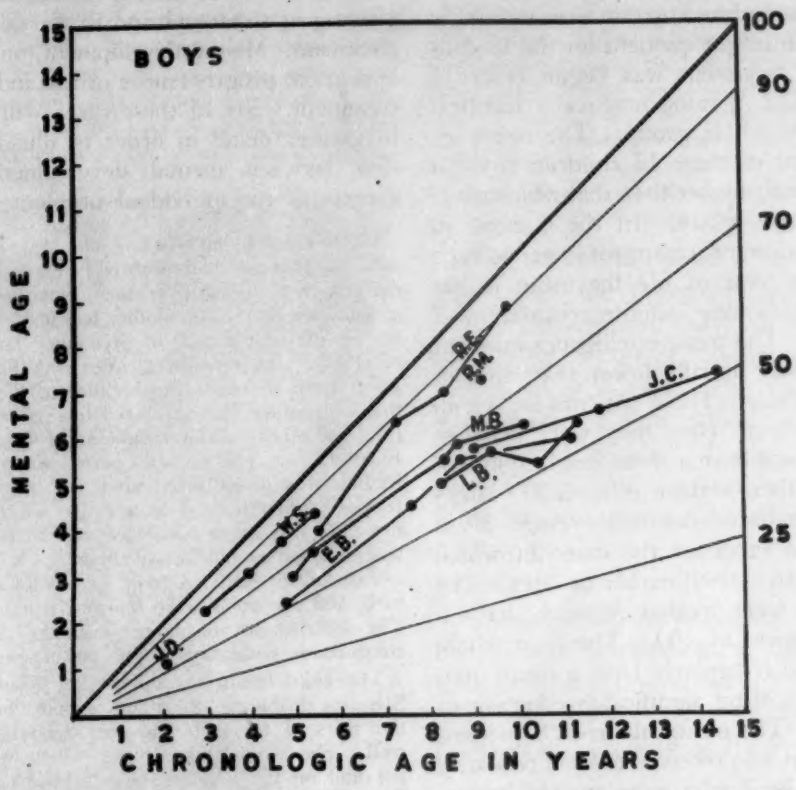

Fig. 1.—Mental ages of 8 hypothyroid boys (cases 3, 4, 13, 15, 16, 17 and 18 in the table; patient "R. M." is not included in the table) compared with chronologic ages.

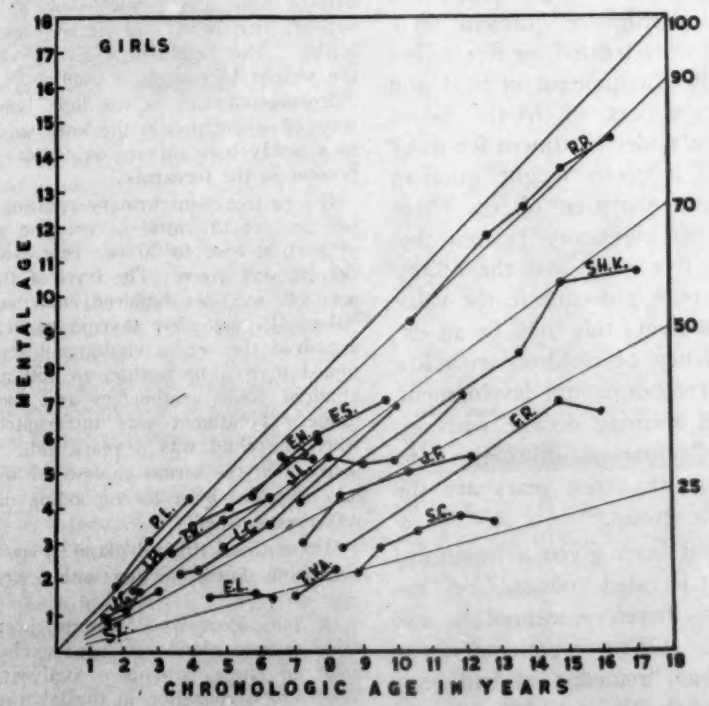

Fig. 2.—Mental ages of 16 hypothyroid girls (cases 1, 2, 5, 6. 7, 8, 9, 10, 11, 12, 14, 19, 20, 21, 22 and 23) compared with chronologic ages.

ning of treatment, the differences between the individual scores within a group are amazingly small. The mean height quotient for the 13 children for whom treatment was begun before 1 year of age is 92.2, a value practically identical with that for the whole group. The mean intelligence quotient of these 13 children is 64, a figure insignificantly higher than that which characterizes the entire group. In the 6 cases in which the initiation of treatment was delayed beyond the third year of life the mean height quotient is 84, indicating definite retardation of statural growth. The mean intelligence quotient is 60, a value only a trifle lower than that of the group as a whole. The 4 patients for whom treatment was begun when they were between 1 and 3 years of age have a mean height quotient of 100; that is, their stature is normal. However, their intelligence quotients average 59, a figure within the range of the cases in which treatment had been started earlier or later. The 16 patients who were treated regularly have a mean height quotient of 100. The 7 to whom thyroid was given irregularly have a mean quotient of 71.5, indicating significant reduction of statural growth. The mean intelligence quotient for the 16 children who received thyroid regularly is 68.4 and for the 7 who were treated irregularly 61.0.

Six patients had been treated for less than five years; for this group the height quotient is 88.8 and the mean intelligence quotient 65.6. The 10 children who were treated for five to ten years have a mean height quotient of 96.4 and a mean intelligent quotient of 64.4. Seven patients who had been under treatment for more than ten years had a mean height quotient of 88.6 and an intelligence quotient of 56. These observations reveal no obligatory relation between the length of treatment and the attainment of height. There is a decline in the value of the intelligence quotient; this may be an expression of the tendency of children with low intelligence to show arrest of mental development. We find, therefore, a seeming decline with advancing age, since, of course, children who have been treated for more than ten years are the oldest members of the group.

Skeletal age has not been given a numerical value in the table but is rated "normal" or "retarded." The results, therefore, cannot be expressed as an average. Of the 5 patients whose skeletal age is rated as "retarded" 4 had been treated irregularly and the fifth had been started on treatment at the age of 8 years.

The survey of this group suggests that physical development, particularly skeletal maturity, stands in distinct relation to the age at the beginning of treatment and to the adequacy of the treatment. Mental development, on the contrary, appears to progress more or less independently of treatment. Six of these cases will be presented in greater detail in order to illustrate the relation between mental development and other aspects of the individual problem.

CASE 1 (table and figs. 3 and 4).—A 5 month old girl, the first child of healthy young parents of Italian descent, was brought to the clinic because of acute cervical adenitis. The mother had had an appendectomy during the first month of pregnancy but had felt well otherwise. In retrospect, after she had subsequently given birth to two normal children, the mother stated that the patient had displayed less intrauterine activity than the others. The weight at birth was 8½ pounds (3,800 Gm.). The neonatal period was normal. Breast feeding was discontinued after two months because of feeding difficulties. The appetite was so poor when the child was given bottle feedings that it was thought that she had trouble in swallowing. Constipation was extreme from birth; a large variety of cathartics were used, and the stools were repeatedly stained with blood. The abdomen became large; even the family noted the conspicuous separation of the rectus muscles.

The child began to support her head at 4 months. She was unable to sit without support but would grasp the sides of the crib and pull herself up moderately well. She would take things which were handed to her and on the whole appeared bright to the mother. She slept well.

The patient exhibited features typical of cretinism—thick skin, yellowish complexion, protruding tongue and umbilical hernia. She was quiet and lethargic. Muscle tone was below normal, but the child could support her head and grasp objects. The cry was husky. The height was 23½ inches (56.3 cm.) and the weight 14 pounds, 5 ounces (6,500 Gm.).

Roentgenograms of the long bones showed that the state of ossification at the knee was approximately that of a newly born infant; no centers of ossification were present in the forearms.

Before treatment urinary creatine constituted only 25 per cent of the total of creatine plus creatinine; the proportion rose to 50 per cent within five days after thyroid was given. The level of the serum cholesterol was 148 mg. per hundred cubic centimeters, and this fell to 101 mg. after thyroid medication. As nutrition improved the serum cholesterol level rose under continued thyroid medication to 150 mg. to 200 mg. per hundred cubic centimeters and fluctuated within this range. Treatment was interrupted for three weeks when the child was 3 years old. There was a rapid increase in the serum cholesterol from 162 mg. to 362 mg., followed by a corresponding drop when treatment was reestablished.

Whole dried thyroid gland[19] was given by mouth in increasing doses, starting with 1 grain (64 mg.) B. P.

19. The Burrows-Wellcome preparation of whole dried thyroid gland was used exclusively in the treatment of these patients. Analyses of the Burrows-Wellcome preparation in the laboratory of the Department of Medicine, Columbia University Medical School, have shown the potency to be approximately one-third that of preparations standardized according to the United States Pharmacopoeia. This accounts for the size of the doses employed.

daily. Within a week the daily dose was 3 grains (192 mg.) B. P. Response to treatment was rapid. The features of cretinism disappeared; the child became more active, ate better and was less constipated. Subsequent dosage of thyroid was regulated by the clinical progress, with the level of cholesterol serving as the index of adequacy. At no time did the patient

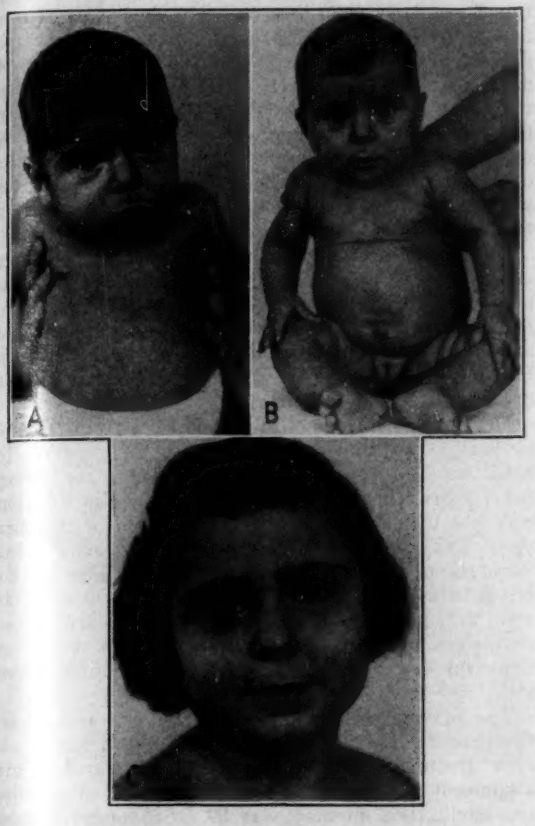

Fig. 3 (P. L., case 1).—*A*, Dec. 5, 1936, age 5 months; *B*, Jan. 16, 1937, age 6½ months; *C*, Dec. 7, 1939, age 3 years and 5 months.

receive more than 6 grains (384 mg.) B. P. a day. Treatment was continuous except when interrupted for observation of the effects of withdrawal on the behavior, the appearance and the level of serum cholesterol. When thyroid was withheld the child became much less active, lost appetite and became constipated.

The cooperation of the family was excellent. Treatment was regular and may be appraised as adequate.

Growth in stature, skeletal maturation and mental development are represented in figure 4. The height became normal and was somewhat above average by the time the child was 18 months old. Retardation of skeletal development was corrected by the time she was 20 months old, and thereafter osseous maturation remained slightly accelerated. She had her first tooth at 10 months. Formal psychometric examination when she was 22 months old yielded an intelligence quotient of 102. A number of less formal observations had already indicated normal mental development. The child sat alone at the age of 10 months, attempted to talk at 11 months and walked at 15 months. When she was 17 months old it was recorded: "She does not differ in behavior or appearance from a normal child of the same age." Progress in mental development was good, and she had an intelligence quotient of 112 at the last determination, at the age of 3 years and 11 months. The patient showed conspicuous willingness to do what she was told, and her coordination was excellent. However, her reaction time was slow, and she became agitated on the suggestion to hurry. She was described by her parents as friendly and outgoing and anxious to be of help to the younger siblings.

This patient has done better than any other member of the group studied. Physical and mental development have progressed satisfactorily. At the age of 5 years she appeared normal in every respect. The diagnosis had been established at 5 months, and treatment had been adequate and regular. The immediate reappearance of symptoms of privation and the rapid rise of the serum cholesterol on withdrawal of thyroid suggest more or less complete lack of thyroid secretion.

One might attribute the good result in physical and mental development to the early and continuous treatment. However, it must be borne in mind that there were signs of adequate motor development (raising of the head at 4 months)

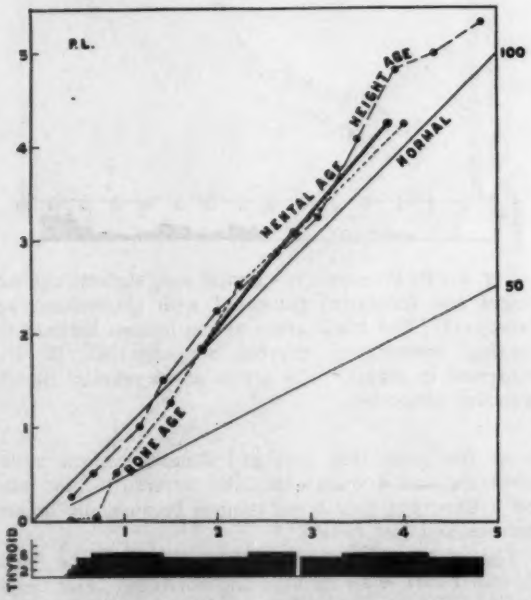

Fig. 4 (P. L., case 1).—Mental age, skeletal age and height age (ordinate) compared with chronologic age (abscissa). The black areas at the bottom indicate the varying amounts of thyroid administered (B. P.), expressed in grains.

and adaptive behavior (accepting things which were handed to her) before treatment was instituted. It seems warranted to interpret these observations as indicating potentially normal mental development before thyroid was given.

CASE 2 (table and fig. 5).—A white girl was first seen at the age of 5 years, 4 months, with the complaint that she was too short, had dry skin in winter and had always been constipated.

The patient was the second child of Russian Jewish parents. The mother spoke English poorly, and it was not possible to obtain an accurate history. The brother, 3 years older, was normal and physically well developed. Pregnancy and delivery had been normal, and the infant's weight at birth was 10 pounds (4,500 Gm.). No abnormalities were noted during the first few months. The child was breast fed until she was 1 year old, with complementary feedings after she was 6 months. She always had a poor appetite and was severely constipated. Urinary continence was established fairly early. The girl began to walk at the age of 18 months and to talk at about 14 months. She was described as a good, obedient child. She had pertussis at 8 months and measles at 1 year, both without complications. Nothing in the history indicates that there had been any sudden change in her development. The parents had been aware of the child's failure to

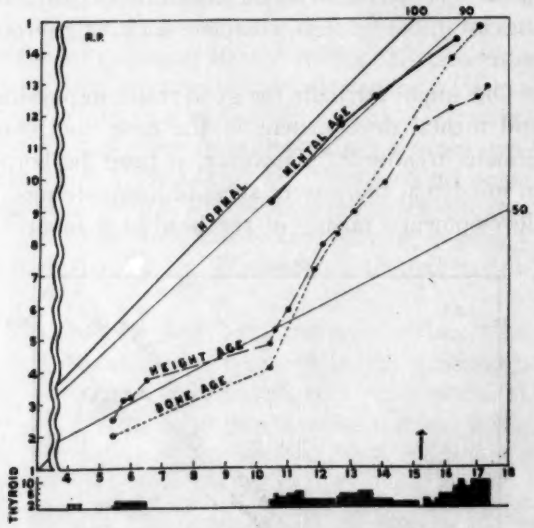

Fig. 5 (R. P., case 2).—Mental age, skeletal age and height age (ordinate) compared with chronologic age (abscissa). The black areas at the bottom indicate the varying amounts of thyroid administered (B. P.), expressed in grains. The arrow at 15 years, 3 months indicates menarche.

grow for some time and had sought medical advice when she was 4 years old. She received "white pills" for a time, but they were stopped because she became nervous and lost weight.

The girl had the typical appearance of the hypothyroid dwarf, with lordosis and pot belly. Her height at 5 years, 4 months corresponded to the average height for 2½ years. The facial features were heavy and the skin dry and thick. The tongue was not protuberant, and the hair was soft and silky. She was described by the examiner as "fairly bright." Psychometric examination was arranged for, but the appointment was not kept.

Roentgen examination of the wrist showed considerable delay in skeletal maturation; the skeletal age was rated at about 2 years. This patient was seen for the first time before we used serum cholesterol and creatine excretion as diagnostic aids. Later on, numerous determinations of the serum cholesterol showed that there were wide fluctuations with changes in the amount of thyroid administered.

Treatment was begun with extremely small doses of whole dried thyroid.[19] One-tenth grain (6.4 mg.) B. P. daily was first prescribed, and the dose was gradually increased to about 3 grains (192 mg.) B. P. per day. In spite of excellent progress, the parents discontinued treatment after one year because of "nervousness." Treatment was resumed four years later and continued regularly from then on. The doses ranged from 3 to 6 grains (192 to 384 mg.) B. P. during the prepuberal period and from 7½ to 10 grains (480 to 640 mg.) B. P. during puberty. In this case the fluctuations in the concentration of serum cholesterol were of great help in determining the amount of thyroid required, particularly during the period of rapid physical development at puberty, when larger amounts of thyroid were needed. Treatment was rated as adequate for the period when given, but irregular.

The response to thyroid medication and to its interruption for four years after the first period of treatment was striking. During the one year of treatment the child grew 3 inches (7.6 cm.). She became brighter and more alert; her skin became soft and thin. Unfortunately there was no reassessment of the skeletal maturation during this year.

During the ensuing four years without thyroid medication the child grew only 3 inches (7.6 cm.). Her height at 10 years, 5 months coresponded to the average for 4 years, 10 months. The skeletal age at this time was less than 4 years. After resumption of treatment there was rapid acceleration of growth and skeletal maturation, as illustrated in figure 5. Menstruation began when the child was 15 years, 3 months old, and the periods were regular. Secondary sexual characters were well developed. Although the patient remained short, she was a well proportioned adolescent girl.

The first psychometric examination was made when the patient was 10 years, 5 months old, a few weeks after treatment was resumed. She displayed mental attainment equal to the age of 9 years, 3 months; the intelligence quotient was 89. Subsequent psychometric examinations showed that she maintained about the same rate of mental development while receiving thyroid. It is to be regretted that no tests had been obtained earlier; repeated appointments had been broken. The patient was of particular interest because she seemed to be intelligent though slow and phlegmatic—this despite irregular treatment and noticeable physical retardation. She attended public school and was able to maintain progress with her class even before receiving thyroid. With treatment she became more attentive and alert. This improvement was continuously bemoaned by her mother as "nervousness." At the age of 16 years she was in the first year of a commercial course in high school. With considerable effort she managed to secure passing marks in most subjects, and she planned to become a stenographer or a dress designer. An effort was made to direct her interest toward some occupation which would demand less speed of mental function and less imagination. The child was socially active, popular with boys and girls and well adjusted in her family relations.

This patient has done remarkably well in spite of having had virtually no treatment until she was 10 years of age—excepting one year of treatment when she was about 6 years old. There is some question whether we are dealing with a case of congenital hypothyroidism. There is no

doubt that the patient suffered from lack of thyroid hormone and that the deficiency was well corrected by treatment. Whether or not the privation was of congenital origin cannot be answered with certainty in view of the inadequate information concerning her early life. There is no indication that some disease had interfered with the function of the thyroid gland during these early years. The retardation in growth was so conspicuous that even her unobservant parents had noticed it before she was 3 years old. Her growth and maturation at the age of 5½ years were not more than those of the average 2 year old child. This severe retardation suggests that the deficiency had been present for a long time and was probable congenital.

Fig. 6 (W. S., case 4).—*A*, June 19, 1936, age 8 months; *B*, July 30, 1936, age 9 months; *C*, Oct. 1, 1936, age 11 months; *D*, June 25, 1940, age 4 years, 8 months.

In contrast to the severe retardation of physical growth and development, there was only moderate delay in the development of locomotor activity and speech. In spite of her sluggishness, the girl did not appear mentally retarded when first examined. With continuous thyroid treatment the mental development, which was normal and in advance of her physical appearance, did not participate in the striking acceleration of somatic maturation but proceeded at the same rate as before. One could argue that this child might have attained a better intellectual level had treatment been instituted earlier. This possibility can be neither denied nor proved. There is no doubt that she was more alert and responsive and better able to utilize her mental endowment when under treatment; yet it appears to us that her intellectual capacity was little if at all affected by thyroid medication.

Case 4 (table and figs. 6 and 7).—A white boy 2 months of age was admitted to the Babies Hospital because of poor appetite and abdominal cramps, with a history of visible abdominal peristalsis noted by the mother. He remained in the hospital for four days, but no diagnostic conclusion was reached. The infant was somewhat irritable, and his muscles were somewhat hypotonic. Cretinism was not suspected, and he was sent home to be cared for by the physician who referred him to the hospital.

The patient was readmitted at the age of 8 months with the complaint of irritability and failure to gain weight.

The patient was the second child of healthy, young parents of Canadian and American descent. One brother, 7 years his senior, was normal. The second pregnancy had resulted in a stillborn child. Pregnancy with the patient had been normal; he was born at term, weighing 10½ pounds (4,800 Gm.). He was not breast fed. The bottle was taken poorly, and the infant seemed to suffer from abdominal cramps and was constipated.

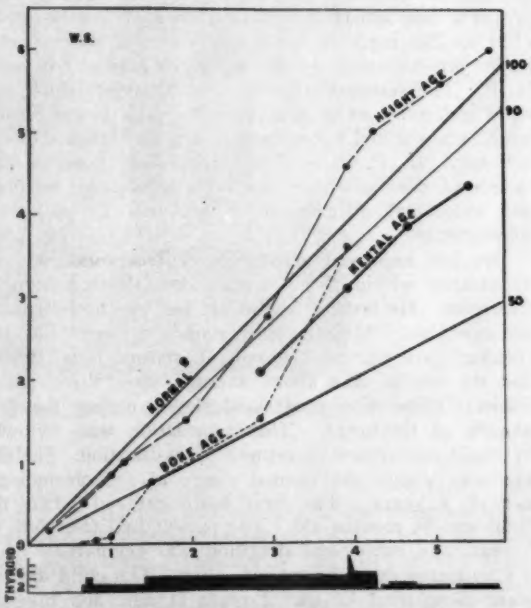

Fig. 7 (W. S., case 4).—Mental age, skeletal age and height age (ordinate) compared with chronologic age (abscissa). The black areas at the bottom indicate the varying amounts of thyroid administered (B. P.), expressed in grains.

Restlessness and irritability were conspicuous from birth; sleep was light and often broken. He was unable to hold up his head or sit alone at the age of 8 months.

On the second entry into the hospital, at 8 months of age, the infant presented obvious features of cretinism, with poor muscular tone and inability to support him-

self. The countenance was characteristic: The eyes were small; the skin was heavy and thick; the hair extended far down on the forehead, and the tongue protruded from the mouth. The fontanels could be felt, and the sutures were readily palpable. The skin exhibited a yellowish pallor. The cry was hoarse.

Roentgen examination demonstrated delay of skeletal maturation. The centers of ossification for the lower femoral epiphyses were just appearing, whereas they are normally evident at birth. There were no centers of ossification in the wrist.

Urinary excretion of creatine was low, only 17 per cent of the total creatinine. Four days after thyroid[19] medication was begun the level of the urinary creatine rose to 49 per cent of the total creatinine, a normal value.

The level of the serum cholesterol was 207 mg. per hundred cubic centimeters at the time the patient was admitted. It fell to 117 mg. after the administration of thyroid. On repeated analyses during the subsequent course it ranged from 150 to 200 mg. per hundred cubic centimeters. When treatment was interrupted, at the time the child was 4 years old, there was a sharp rise from 153 to 400 mg., and a rapid fall to the previous concentration took place when treatment was resumed. This behavior suggests virtually complete lack of thyroid secretion. The immediate reappearance of clinical hypothyroidism when treatment was suspended leads to the same inference.

Thyroid medication was begun as soon as the clinical diagnosis had been confirmed by laboratory data. Treatment was continuous except for deliberate interruption for special observations. During the first three years progress was satisfactory with a dose of 2 to 4 grains (128 to 256 mg.) B. P. a day. For a short period larger amounts were given—up to 10 grains (640 mg.) B. P. The severe disturbances of behavior which this child exhibited were aggravated by the larger doses, which necessitated a decrease to 1½ to 2 grains (96 to 128 mg.) B. P. daily. The regulation dose in this case was determined by special attention to behavior and emotional adjustment. This will be discussed subsequently.

The boy improved greatly in general condition and appearance within a few weeks after the initiation of treatment. He became less placid but was not normally self-assertive. Muscle tone remained poor for the ensuing two years. Growth in stature was steady, and the height was above average after three years. Skeletal maturation progressed slowly during the first months of treatment. This retardation was followed by rapid appearance of centers of ossification. Skeletal age was within the normal range at the chronologic age of 4 years. The first tooth erupted when the child was 10 months old. The patient had five teeth at 1 year, and subsequent dentition was regular.

Locomotor development was slow. The child did not walk alone until he was 2 years of age, and his gait remained somewhat awkward even at 5 years. The awkwardness became more conspicuous when he was not taking thyroid. He began to talk at 23 months and soon learned to articulate well.

Since the family lived at a distance the boy was not seen with the frequency rendered desirable by recognition of the fact that he presented a behavior problem of a nature not seen in any other of our hypothyroid patients. When he was 2 years old he looked intelligent and was attentive, but his habitual behavior was so uncontrollable and negativistic that no appraisal of mental capacity could be made. The mother complained of his destructiveness and disobedience. A psychometric examination when he was 2 years, 11 months of age could not be completed because of poor cooperation. He sometimes responded to test questions; at other times he would either refuse to look at the test material or demand to keep the objects and would scream loudly if an effort was made to take the things away from him. He passed the tests for 2 year old children except that he was unable to point out the parts of his body, although the mother expressed confidence that he knew them.

He was not seen during the ensuing year. The mother brought him back because he had become so unmanageable and antisocial that she was unable to cope with him. After having become continent he had recently begun to soil himself. The association of this lapse into incontinence with uncontrollable behavior was interpreted as indicative of mental defect in consequence of inadequate thyroid treatment. With the patient under observation in the hospital, the amount of thyroid was increased. It soon became clear that the boy's behavior became worse with the increasing doses. Since his physical development was satisfactory, after a short period without thyroid he was continued on the lowest dose which prevented symptoms of somatic hypothyroidism. A pneumoencephalogram taken while he was in the hospital revealed that the gross architecture of the brain was entirely normal. Psychometric examination yielded an intelligence quotient of 79.

During the next year the behavior of the child was less troublesome, and he was well adjusted in kindergarten. When he was 5½ years old he again became so aggressive and destructive that he was admitted to the children's psychiatric ward of Bellevue Hospital for observation under the supervision of Dr. Lauretta Bender. Bellevue has courteously reported that "he adjusted himself well to the ward routine, was happy, smiling and joined in group activities. He was able to take care of himself except that he needed some help in dressing. He was active, talked incessantly and was quite boisterous in his play. On the whole he was considered to be a happy, friendly and cooperative child." During his stay in Bellevue he was given two psychometric examinations, the first while he was receiving thyroid and the second after he had been without it for a month. Although the physical features of hypothyroidism reappeared and although he showed considerable slowing of activity and speech, the two examinations showed almost identical results: The first intelligence quotient was 81 and the second 83. These values are congruent with those obtained earlier at the Babies Hospital. The only evident difference was in the quality of his drawings. We attach significance to the fact that they became less erratic and better integrated after he had been receiving no thyroid for a while.

Investigation of the home revealed that the child had been exposed to unusual tension and strife between the parents. The recent outburst of destructiveness had arisen after the parents had finally separated and the mother had moved to New York with the patient and his elder brother.

We interpret the behavior difficulties of this child as neurotic; his insecurity at home was evidently an important contributory factor.

Although the patient did not present obvious signs of cretinism when 2 months old, there can be no doubt that he was classically hypothyroid. He probably suffered from complete lack of functioning thyroid tissue. The considerable delay in skeletal development, the prompt response

to thyroid treatment and the relapse after its withdrawal all strengthen this conclusion.

Physical symptoms disappeared promptly after the initiation of thyroid therapy, and the growth deficit was corrected when he was 3 years old. Skeletal maturation was somewhat delayed, but the bones had attained normal dimensions by the fourth year.

Intellectual development as assessed from clinical observations and by formal tests showed even progress at a dull normal level. The intelligence quotient, determined at various times over a representative period, was approximately 80. There was always a question whether the serious emotional disturbances which resulted from environmental causes interfered with his best use of native intellect. However, it is doubtful that even his best achievements would surpass the dull normal level.

This case is particularly instructive because the patient was the only cretin in our experience in whom an aggressive behavior disorder developed. Once they are adequately treated, hypothyroid children present few problems of management. They are usually docile, easily led and satisfied within the narrow realm of their limited capacity. If the environment is inadequate and begets insecurity, they may react with signs of anxiety, but they do not ordinarily become aggressive. A severe aggressive disorder such as this boy showed is exceedingly rare. We know of no report of a case of this sort in the literature.

It should be noted that, for the optimal treatment of the child and the proper adjustment of the total situation, it was necessary to make a clearcut distinction between retardation of development and emotional disorder. Increase in the amount of thyroid administered produced more severe symptoms. Study of this case suggests that the largest dose which can be tolerated without producing obviously toxic symptoms is not always the optimum for procuring integrated mental and emotional function.

Fig. 8 (M. B., case 13).—*A*, Dec. 8, 1932, age 2 years, 8 months; *B*, Nov. 20, 1933, age 3 years, 7 months; *C*, April 2, 1940, age 10 years.

CASE 13 (table and figs. 8 and 9).—A boy 2 years and 8 months old was brought to the clinic because of retarded development, especially with regard to speech and locomotion. The family had been aware of this since the child was 14 months of age. They thought that he had progressed normally as an infant.

The patient was the only child of young Jewish parents who were cousins. They had separated shortly after his birth, and he had been cared for by his maternal grandmother. The pregnancy and delivery had been normal, and the condition of the infant at birth had been good; the weight at birth was 7 pounds (3,200 Gm.). He had been breast fed for one month and then had received the bottle. The appetite had always been poor, and he was an irregular eater. At 2 years, 8 months he refused all solid foods and was therefore fed soup and milk from a bottle. He had always been constipated. Control of urination and defecation had not been established.

According to the grandmother progress had been "normal" up to the age of about 8 months; the child then failed to develop and appeared to regress. He had sat up at the age of 5 months but did not walk until he was 2 years old; even at 2 years, 8 months he had an insecure gait. The first tooth erupted when the child was 13 months old. He began to say "words" at the age of 9 months but made no progress thereafter. He made signs to indicate his wants. The grandmother was certain that he grasped what was said to him. According to her he was "intelligent and active" and "would play as much as other children of his age."

In contrast to the foregoing view, we found the child to be seriously retarded physically and in all developmental achievements. He was extremely sluggish, both physically and mentally. He was short and thickset and had severe lumbar lordosis. His gait was waddling, and he required support. The skin was dry, thick and cool, and there was noticeable hypertrichosis. The face was that of a typical cretin, with a thick

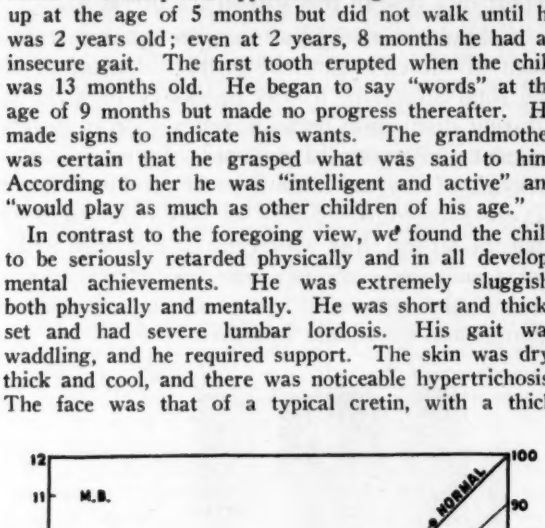

Fig. 9 (M. B., case 13).—Mental age, skeletal age and height age (ordinate) compared with chronologic age (abscissa). The black areas at the bottom indicate the varying amounts of thyroid administered (B. P.) in grains.

tongue. He had only five teeth, and the anterior fontanel was still open. He was unable to speak.

Roentgenographic examination of the skeleton showed conspicuous retardation of ossification in the short bones of the skeleton and failure of normal fusion of the sutures of the skull. A point of special interest was the failure in proportionate growth of the upper portion of the thorax despite the robust appearance of the child. This feature was ascribed to defective longitudinal growth of the ribs, similar in nature to the retarded growth of the extremities. The skeletal age was rated at about 6 months.

Studies of creatinine and cholesterol were not made at the time when the patient was first examined. Almost daily measurements of the change in the proportion of creatine excreted and in the level of the serum cholesterol were made for four months when the boy was 8 years old. The effect of the withdrawal and resumption of administration of thyroid was studied during this period. The level of the serum cholesterol, which had ranged previously between 150 and 170 mg. per hundred cubic centimeters, rose rapidly within three weeks to 525 mg. and then fluctuated around this level. Following the administration of thyroid there was a sharp drop to 150 mg. While the patient was under treatment the creatine excreted had amounted to about 40 per cent of the total creatinine. It dropped to below 10 per cent during the first month after thyroid was withheld and rose to approximately 18 per cent during the second month. When thyroid was given again the creatine excretion rose to above 50 per cent of the total creatinine and then dropped to the previous level of 40 per cent. These data are evidently consistent with a diagnosis of athyreosis.

Whole dried thyroid gland[19] was given in amounts varying from 5 to 10 grains (320 to 640 mg.) B. P. daily. Treatment was interrupted several times for special studies. The longest period without thyroid was three months, when the boy was 8½ years old. The previously mentioned observations on cholesterol and creatine were made at this time, together with studies of the changes in physical appearance, behavior and intellectual activity. Except for these experimental interruptions treatment was both regular and adequate.

The behavior and appearance of the child changed dramatically after thyroid therapy was begun. After a few days he became more playful and looked happier. The cretinoid features disappeared within a few weeks, and the rate of physical growth and development accelerated. Skeletal maturation had become normal by the time he was 3 years, 8 months old and progressed at a normal rate thereafter. It took longer to make up the height deficit; at the age of 11 years the patient was of low average height.

The first psychometric test was made when the child was 5 years old. His mental age at that time was 3 years; his intelligence quotient, 60. Previous clinical observation had indicated that he was seriously retarded in spite of the greater alertness which had followed treatment. On subsequent examinations his intelligence quotient ranged between 56 and 66. The results seemed to depend somewhat on the attentiveness of the child.

Of peculiar interest were observations of his intellectual function which were made while he was being treated with thyroid at the age of 8 years, 4 months, and after the treatment had been discontinued for three months, when he was 8 years, 7 months of age. At the time of the first examination the psychologist noted that he "was a very active child, whose attention it was impossible to keep centered on a task more than a few seconds without constant reminders and urging. However, he was very much interested by all the test materials and at all times appeared to make a good effort to do what was asked of him. He had a rather bad speech defect which made it difficult at times to understand his responses. He was very restless and kept jumping up to get materials which were out of his reach or to inspect something which attracted his attention." His mental age at that time, according to various tests, was 5 years, 6 months; his intelligence quotient, 66. Three months later, at a time when he showed the full-fledged picture of thyroid deficiency and when the level of the serum cholesterol was 531 mg. per hundred cubic centimeters, the psychologist made the following comment: "The boy cooperated very well today. There was no difficulty at all in keeping his attention on the tasks. He was pleasant, smiled in response to praise and was attentive. He was somewhat phlegmatic in his general behavior, but his effort was persistent and good. With the exception of a few instances his speech was easily understood. There was no trace of the restlessness which characterized his behavior in July. In fact, once the boy settled down in

his chair he remained there apparently contented until the tests were over. He enjoyed the tests and himself asked for more 'games.' He seemed to be under no emotional tension at all. On the contrary, he was calm throughout the examination. The test results can be considered reliable." His mental age was now 5 years, 10 months; his intelligence quotient, 68. The results of the two examinations were compared by Dr. Z. Piotrowski: "There is no difference as far as the results pertaining to the level of native intelligence are concerned. The difference between the intelligence quotient of 66 obtained in July and the present intelligence quotient of 68 is not significant. The vocabulary and the free drawings are the same as far as the scoring is concerned. There was some improvement in these tests, but this referred only to the manner of going about solving the tests rather than to the final achievement. The Pintner-Patterson performance test, however, showed a marked improvement. It is known reliably that the degree of nervous tension or emotional disturbance appreciably affects the performance on mechanical tests. It is reasonable to assume that the improvement in these tests is due to improvement in personality which has taken place since July. This conclusion is confirmed by the differences in attitude which the boy showed on the two different examinations as well as his free drawings. Although the number of details which determine this score according to the Goodenough scale is the same, the difference in the quality and lines is great. In July the lines were angular and irregular. Today they are much firmer, not fantastic, and the face was roundish instead of being boxlike as previously. The lines do not overlap, nor are there any gaps left between them. The comparison of the boy's drawings in July and in October reveals admirably the difference which seems to have taken place in the child's personality as far as the tests can reveal it: The intellectual capacity has remained the same (high grade defective), but it is being used now with much greater efficiency than it was before."

The boy was cared for during the early years by his grandmother. Later he lived in an orphan asylum or was placed in foster homes. The mother was always willing to leave him in the hospital for study. In contrast to the boy described in case 4, this child was docile and friendly in spite of poor home care. His sleep was restless at times, and he was irritable and would fight with the younger children. These symptoms disappeared when the dose of thyroid was decreased. Since his height was subnormal, the dose was kept high for a considerable time. An additional impetus for the maintenance of high dosage was the vain hope of improving the mental capacity of the patient.

The history as supplied by the grandmother would lead one to expect a physically retarded but otherwise intelligent and active boy, save for the fact that he could not talk. Examination revealed him to be seriously retarded mentally and extremely sluggish. This case illustrates, among other things, the unreliability of the information about the early development of a condition given by the family of a patient.

Response to treatment was prompt; physical improvement was striking. The intellectual development, once the sluggishness had been corrected, proceeded at the same rate as before treatment. It remained that of a moron.

Of outstanding interest is the observation that the performance of skilled acts was better after the patient had received no thyroid for a while than it was while he was receiving a dose which was probably too large. This was the first time that we had encountered this phenomenon; furthermore, we had not—nor have we since—found mention of it in the literature. Hence we paid less attention to it at the time than we would now, having made the same observation in other cases. Given another opportunity, we should employ smaller doses, amounts which would ensure normal somatic development but which would not produce exaggerated functional tension. This observation illustrates the fallacy of expecting improvement of intellectual capacity

Fig. 10 (S. C., case 22).—*A*, June 12, 1936, age 8 years, 2 months; *B*, Oct. 19, 1936, age 8 years, 6 months; *C*, Nov. 9, 1937, age 9 years, 7 months.

from increasing the dose of thyroid beyond that required for adequate physical progress. Excess thyroid not only fails to improve the rate of mental development but actually interferes with the efficiency with which intellectual abilities can be utilized.

CASE 22 (table and figs. 10 and 11).—A girl aged 8 years, 2 months came to our attention because of mental retardation. She had received irregularly some kind of treatment, the nature and amount of which are not known. She had taken no medicines during the preceding six to eight months.

The patient was the fourth child of Jewish parents who were about 40 years old at the time of her birth. Three older siblings were of normal physical makeup and intelligence. The patient weighed 8½ pounds (3,900 Gm.) at birth and developed well up to the age of 5 or 6 months. She then showed increasing signs of mental and physical retardation: Locomotor develop-

ment was much delayed; she did not walk until she was 5 years old. She began to use single words at 4 years but was unable to form sentences. The mother described her as a happy child who seemed to understand simple commands. The patient had always been hard to feed because of difficulty in swallowing. She had always been constipated. Toilet habits had not been established.

The child was broad and short, and her gait was insecure and waddling. The skin was dry and hairy. The face was broad, with heavy features and thick lips and tongue (fig. 10). The teeth were all of the deciduous dentition. Mentally she was extremely retarded, speaking only a few words in a hoarse voice and crying frequently.

Osseous development was seriously delayed; her skeletal age was placed at 4 years.

Studies of the cholesterol level and creatine excretion under the influence of thyroid and after its withdrawal have been published previously.[20] Observations on

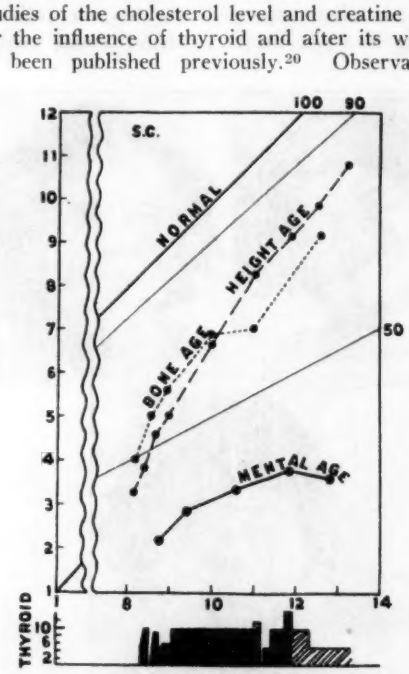

Fig. 11 (S. C., case 22).—Mental age, skeletal age and height age (ordinate) compared with chronologic age (abscissa). The black areas at the bottom indicate the varying amounts of thyroid administered (B. P.), expressed in grains.

this patient as "a typical cretin" were compared with those on a child on whom complete thyroidectomy had been performed for carcinoma of the gland. The data were characteristic of an athyroid state.

Whole dried thyroid gland [19] was given in doses of from 5 to 10 grains (320 to 640 mg.) B. P. daily. Except during short periods used for study, thyroid was given regularly and in adequate amount, as checked by physical progress and concentration of serum cholesterol, until the patient was about 12 years old. After that time treatment became irregular because the child refused the tablets frequently.

The changes in the appearance and disposition of the child were spectacular. Within two weeks after the administration of thyroid was started she was laughing and talking with the other children in the ward. She ate better and seemed to understand more readily. Urinary continence was established within the next few weeks. Physical progress was satisfactory. Her height, which was that of a 3¼ year old child when treatment was begun, increased at about twice the normal rate during the first year of treatment and then at a rate which was slower but still in excess of the normal increment. Skeletal maturation showed similar rapid progress. The growth deficit, however, had been so severe that the child had not yet attained normal height when she was 13 years of age. She was still growing at that time and showed the first signs of puberty.

Estimation of mental age was not attempted until several months after treatment had been started and after the patient had become more responsive, at the age of 8 years, 10 months. On the Merrill-Palmer scale her mental age was 2 years, 2 months and her intelligence quotient 24. She obtained a slightly higher rating during the following years, that is, 30 and 31. Her mental age on the last examination, at the chronologic age of 12 years, 10 months was 3 years, 7 months according to the Stanford-Binet test (intelligence quotient, 28) and 3 years, 2 months on the Merrill-Palmer scale (intelligence quotient, 24). These comparisons indicate that her intellectual growth had not participated in the increase in rate shown by her physical development. Yet there is no doubt that the child benefited mentally from treatment. She became more responsive and affectionate, was trained to toilet habits and enjoyed playing with children much younger than herself.

There is no question but that this patient suffered from congenital complete athyreosis. The presence of recognizable symptoms as early as at the age of 5 months and the serious retardation of growth and skeletal maturation point to this conclusion. It is not known whether there had been any replacement therapy before the child was 8 years old. If there had been any at all it was certainly grossly insufficient and irregularly administered.

Mentally the patient was also seriously retarded—even more than physically. The degree of physical retardation was of the same magnitude as in the girl reported in case 2. In both instances the statural and skeletal ages were less than half the chronologic ages. In both there was rapid acceleration of physical development following thyroid medication. The intellectual development proceeded at about the same level during the period of treatment as prior to it, with the difference that in the patient described in case 2 this level was low normal (intelligence quotient, 90) and in this girl, whose intelligence quotient was about 26, it was that of a high grade imbecile. Though both children benefited from treatment, becoming more alert and responsive, their actual intellectual capacities remained entirely uninfluenced by treatment with thyroid. The comparison of the 2 cases illustrates graphically the fact that intellectual development in the hypothyroid child may progress independently of physical development and thyroid medication.

20. Langmann, A. G., and Bruch, H.: Carcinoma of the Thyroid Gland in Children, Am. J. Dis. Child. **56:** 616 (Sept.) 1938.

CASE 23 (table and figs. 12 and 13).—A girl 9 months old was brought for examination because of a cutaneous eruption of six weeks' duration. The mother had not recognized that the child was retarded or, for that matter, that she was unusual in any way. The mother had worked as a seamstress until the end of pregnancy. She had no specific difficulties during the pregnancy but was constantly tired and lost her appetite. She lived on coffee and rolls, so that the gain of weight during pregnancy fell about 10 pounds (4.5 Kg.) short of what might have been expected. After delivery her health improved, but she did not again become pregnant.

The child was so inactive during intrauterine life that fetal movements were not noticed until at the end of pregnancy. Birth occurred at term after labor of one hour. The infant was cyanotic and was given a blood transfusion. There were no signs of cerebral injury and no stupor or convulsions. She was kept in an incubator for four weeks. The infant was jaundiced when she left the hospital. She was never fed at breast.

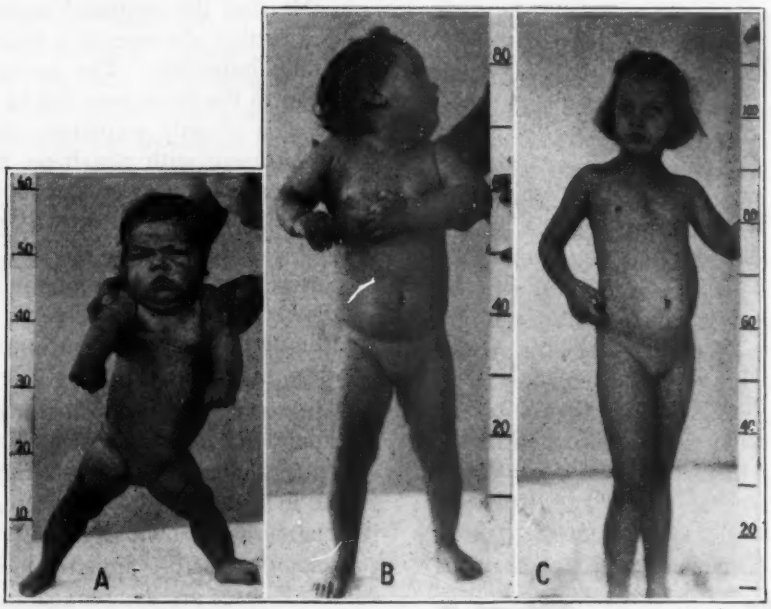

Fig. 12 (E. L., case 23).—*A*, Nov. 11, 1935, age 9 months; *B*, Jan. 8, 1937, age 2 years; *C*, Dec. 14, 1940, age 5 years, 11 months.

The baby was quiet and slept most of the time, crying only when hungry. She could hold up her head by the time she was 9 months old, but she was unable to sit up and paid no attention to the environment. She had never reached for or grasped anything. The mother described her as "a very good baby."

When the patient was first examined (9 months) she looked like a cretin (fig. 12), with a flat, broad face and thick, dry skin. There was eczema on the face and arms and in the groin. The fontanels were open and the sutures palpable. No teeth were present. Muscle tone was poor, and the child could support her head only with difficulty. Mentally she was apathetic and dull, and she did not respond when spoken to.

Roentgen films of the skeleton showed severe retardation; the state of ossification was approximately that of a young premature infant.

The cholesterol content of the serum was not determined before treatment was begun. Later measurements revealed the characteristic fluctuations in response to the administration and withdrawal of thyroid. Under adequate treatment the cholesterol content of the serum varied between 140 and 190 mg. per hundred cubic centimeters. Interruption of treatment when the patient was 5 years old was accompanied by a rise to 446 mg. Four weeks after treatment was resumed the cholesterol level was 190 mg.

Thyroid[19] was given in amounts which varied between 1 and 6 grains (64 and 384 mg.) B. P. daily. The immediate response was striking. Within two weeks the cretinoid features disappeared, while activity and appetite increased. Two months later the patient was evidently much improved. She looked at books and dolls and produced some sounds. She was able to hold her head well but could not sit alone. The first tooth appeared when the child was 11 months old.

Physical development progressed satisfactorily. Within four months the stature of the patient reached the average for her age and then surpassed it. The skeletal maturation was also greatly accelerated. The skeletal age of the patient became normal by the time her chronologic age was 17 months. When the child was 2 years old she was taken to Germany for a visit with the grandparents; there she stayed for more than two years. Treatment was continued most of the time. The mother did not know the exact amount administered. The child received no thyroid during the last three or four months preceding her return to the United States. Since growth in length and skeletal maturation progressed at normal rates during her absence from the United States, it is a fair presumption that treatment during this period was adequate except for the interruption preceding return to this country.

Mental development did not keep pace with somatic acceleration. After the initial improvement there was little progress, and the child showed such meager response to and interest in her environment that the question was repeatedly raised whether she could hear and see. As far as could be determined there was no defect of these senses. She learned to walk when she was between 3 and 4 years of age, but her gait was still insecure when she was 6. She devised a "speech" of her own, making certain noises to indicate different wants; to these the mother responded. When in

Germany she learned a few words like *Mama, Papa, bitte* (please) and *Puppe* (doll).

The first psychometric examination was made when she was 4 years, 6 months old. Her achievement was meager. She did not succeed in passing any of the tests at the 2 year age level of the Stanford-Binet scale, and her motor development on the Kuhlman-Binet scale was at the level of 18 months. These responses indicate a high degree of intellectual deficiency such as is described by an intelligence quotient of about 33. When reexamined fifteen months later, at the age of 5 years, 9 months, her performance was on the same level, of approximately 18 months; there had been some progress in hand-eye coordination. In the next year, when she was 6 years, 4 months old, her rating on the Kuhlman tests for infants was only 16 months. She passed no test item above the 18 month level. The intelligence quotient was 21.

The child was characteristically restless, and she continually performed such stereotyped movements as rocking back and forth or running around. She paid no attention to other children. She liked to listen to radio music, and the mother reported that she was able to hum the tunes of several songs. The mother interpreted her inability to follow commands as stubborn disobedience. The patient could drink from a glass, and she tried to feed herself but made no attempt to dress herself. Toilet habits were fairly well established by the time she was 6 years old, although she wet herself occasionally.

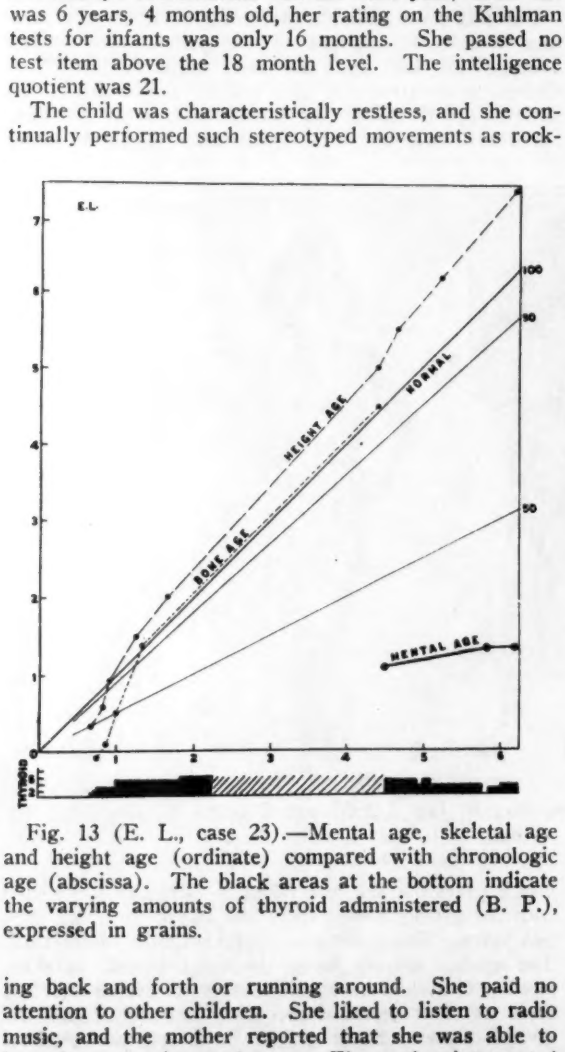

Fig. 13 (E. L., case 23).—Mental age, skeletal age and height age (ordinate) compared with chronologic age (abscissa). The black areas at the bottom indicate the varying amounts of thyroid administered (B. P.), expressed in grains.

A pneumoencephalogram made when the child was 6 years of age showed what appeared to be a considerable difference in the size of the lateral ventricles with dilatation of the left ventricle.

The outstanding feature of this case is the conspicuous discrepancy between satisfactory physical progress and arrest of mental development at an exceedingly retarded stage. At 6 years of age the girl looked perfectly normal at the first glance, and she would have been a pretty child but for the emptiness of her countenance. Increase of activity when treatment was begun inspired the hope of significant improvement. Real progress and acquisition of new functions were, however, exceedingly slow, and there was no further development of intellect after the third or fourth year. On three subsequent examinations about one year apart her meager achievement remained below the 18 month level.

There is little doubt that this child had a defective brain which could respond to thyroid only within restricted limits; no development beyond its capacity to mature could be expected. It is possible that the postnatal anoxia and jaundice added further damage to a brain that was congenitally imperfect. The question whether the damage to the brain was due to dysgenesis or to trauma is of only secondary importance to the main problem with which we are concerned in this paper, namely: Can thyroid medication influence the innate mental capacity of a hypothyroid child?

Severe mental retardation had been foreshadowed by the extremely low degree of spontaneous locomotor function during the first nine months of life.

The retardation of locomotor development and of adaptive behavior in this child stands in contrast to the relatively good functional development in the girl who was described in case 1; the latter had shown signs of potentially normal development before any treatment was supplied. These 2 cases are comparable as far as early beginning and adequacy of treatment are concerned. The physical development was equally satisfactory in the two instances. The extreme difference in intellectual development cannot be correlated with adequacy of treatment but has to be considered as an expression of difference in innate intellectual capacity or degree of cerebral development independent of the hypothyroid state of extrauterine life.

COMMENT

The aim of this inquiry is to evaluate the effect of adequate treatment as judged by physical progress on the mental development of congenitally hypothyroid children. Our observations lead to the conclusion that mental capacity shows noteworthy independence of the amount of treatment. The question can, of course, be raised whether a child whose treatment was delayed might not have done better had therapy been

started at an earlier age. This possibility can be neither affirmed nor denied on the basis of our material.

Results similar to those presented in this paper have been recorded by only a few observers.[1] The prevailing opinion concerning thyroid therapy is optimistic. However, the accepted generalizations are not based on longitudinal data; on the whole, they rely more on personal impression and hope than on quantitative measurement.

The observations of Gesell and his co-workers showed that the initial response to treatment served as "an index of the reserve capacity" for mental development and provided a basis for prognosis. All of their patients had been observed since early infancy. Since our patients came for treatment at various ages—some as advanced as 8 years—we were able to accumulate data on the developmental achievement before treatment. Thus our data have brought to light the previously unrecognized fact that the functional development before treatment supplies an index of the capacity for future mental development. The common description of congenital hypothyroidism contains the statement that all developmental achievement is noticeably delayed. It is our experience that those children who have the capacity for good intellectual development are much less retarded than those whose subsequent progress will be poor; careful appraisal of the degree of retardation will allow a tentative prophecy of the ultimate level of achievement. If spontaneous development without thyroid is seriously retarded there appears to be little chance to attain a normal state with thyroid; accordingly, the physician must be guarded in prognosis lest he encourage parents to expect a better result than can possibly be achieved.

Another observation not previously recorded in the literature is that an excessive dose of thyroid is not without harm even though no somatic toxic effects are observed. When taken in an amount greater than that required for satisfactory physical growth, thyroid seems to have a disrupting effect on the function of the total personality. Attempts to improve poor mental development by the administration of thyroid beyond that which is actually required for normal physical maturation not only fail to improve the mental capacity but even make for poorer adjustment and function of the already handicapped child. Our clinical impression that this was so has been corroborated by measuring accomplishment by several psychometric tests. It was found that integrative function was improved when excessive doses of thyroid—albeit not large enough to produce obvious toxicity—were reduced to lower levels.

These conclusions do not detract from the importance of diagnosis and treatment of hypothyroidism at as early an age as possible. All children were easier to manage and played a more constructive role within the family group when given adequate amounts of thyroid. In general, these children were good natured and exhibited great emotional warmth; the patient described in case 4 was the only exception. Many children showed restlessness, irritability and coincidental behavior difficulties when given too much thyroid; they also became irritable if treatment was interrupted. It would appear that an optimal intake of thyroid is necessary for harmonious function; the amount required varies from person to person and must be determined by trial.

The demonstration of poor correlation between the time of beginning treatment and the dose of thyroid, on the one hand, and the ultimate mental capacity, on the other, suggests that the changes in the brain which are responsible for the mental defect take place during prenatal life and are not the sequels of postnatal hypothyroidism. The common coincidence of mental defect with congenital hypothyroidism suggests that both organs, the thyroid gland and the brain, are affected harmfully during the formative stage. The frequent assumption that maternal hypothyroidism is the cause of the defect cannot be sustained since most of the children who later exhibit these conditions are born without manifest signs of hypothyroidism. It is conceivable that severe malnutrition on the part of the mother during pregnancy is the agent of damage; this is suggested by several cases in our series. The possibility is supported by the demonstration that other malformations[21] can be produced by this means. Whatever the harmful influence is, it does not necessarily affect both brain and thyroid gland; otherwise, normal mental development would never take place in persons with congenital hypothyroidism. By the time of birth the potentiality for mental development has become independent of the activity of the thyroid gland. Whether this inherent capacity will be realized and mental endowment utilized to the fullest measure is, however, dependent on adequate treatment of the hypothyroid state.

SUMMARY

The administration of thyroid restores the growth and development of the congenitally hypothyroid child in a highly gratifying way. The consistency of this effect has fostered the pre-

21. Warkany, J., and Nelson, R. C.: Congenital Malformations Induced in Rats by Maternal Nutritional Deficiency, J. Nutrition **23**:321, 1942.

vailing view that if treatment is begun early enough and continued in adequate amount satisfactory mental development can be anticipated in nearly all, if not all, patients. As a corollary, failure to attain this result is ascribed to delay in treatment or to the use of insufficient doses. This opinion can be traced back to the early literature on the subject; it continues to be echoed by contemporary writers. There is, however, considerable evidence that the correlation between the quantitative aspects of treatment and the final state of intelligence is far from perfect. From time to time observers have expressed disappointment with the mental development of patients whose physical progress left little to be desired. The discrepancy between success in promoting somatic improvement and achievement with respect to mental progress has been brought out in a more precise way by a small number of recent studies.

The observations reported in this paper have persuaded us that one must observe caution in predicting the intellectual future of congenitally hypothyroid children, irrespective of both the time at which treatment is first instituted and the adequacy of the treatment as judged by physical criteria. This opinion is based on a statistical examination of the data from longitudinal studies of 23 cases of the disorder. Whereas these observations demonstrate a distinct relation between early, adequate treatment and subsequent physical development, they show that a comparable relation is absent, or at most highly imperfect, with respect to mental attainment. This prompts the inference that the intellectual inferiority presented by many congenitally hypothyroid children is not in all cases due to lack of thyroid hormone; it appears likely that in some instances at least there is a concomitant defect of cerebral development which cannot be modified by glandular treatment. It is, of course, conceded that in other cases retarded growth of the brain may be due to postnatal lack of thyroid; hence no impulse is felt to belittle the importance of early diagnosis and treatment.

Two conclusions emerge with reasonable clarity from our observations: First, the prognosis for intellectual development must necessarily be guarded in advance of therapeutic trial. In this respect information regarding the rate of spontaneous functional progress before treatment supplies a fairly reliable basis for prediction—much more informative than mere knowledge of the time at which the administration of thyroid was first started and of the apparent sufficiency of the dosage. Second, too vigorous use of thyroid can have distinctly undesirable consequences. Deterioration of performance quantitatively measurable by psychometric tests may take place when excessive amounts are administered. Whereas intensive treatment is warranted during a trial period, the fact must be kept in mind that overdosage can give rise to serious disorders of behavior. Unless such dosage is clearly productive of proportionately improved mental development the social and emotional problems which it may engender must not be ignored.

3975 Broadway.

Abstracts from Current Literature

Metabolism; Infant Feeding; Milk and Other Foods

THE RELATION OF MATERNAL DIET TO BREAST FEEDING. J. H. EBBS and HELEN KELLEY, Arch. Dis. Childhood **17**:212 (Dec.) 1942.

The authors compare the incidence of breast feeding in three groups of mothers of the low income class. Those who were supplied with extra food and those who were educated to provide a good antepartum diet were more successful in nursing their infants than those mothers who had been left on their usual poor prenatal diets. The effect of postpartum diet on nursing was evidenced by a decrease in the percentage of breast-fed babies when the giving of extra food was stopped six weeks after the birth of the baby. The relation of poverty to poor antepartum diets and its effect on the incidence of breast feeding and the development of the infant are pointed out.

KELLY, Milwaukee.

THE INCIDENCE AND MORTALITY OF BREAST- AND ARTIFICIALLY-FED INFANTS ADMITTED TO HOSPITAL WITH INFECTIONS. J. H. EBBS and FRANCES MULLIGAN, Arch. Dis. Childhood **17**:217 (Dec.) 1942.

In reviewing the case histories of 1,500 infants under 1 year of age, admitted with infections to the Hospital for Sick Children, Toronto, during three and a half years, evidence was found that fewer breast-fed babies were admitted than artificially fed babies. The incidence of breast feeding among the 1,500 patients admitted with infections was less than half the incidence of breast feeding in the well baby clinics in the city. Infections of the respiratory tract were found more frequently than other types. The incidence of gastro-intestinal infections was lower in the breast-fed babies. The mortality was slightly higher in the breast-fed group.

KELLY, Milwaukee.

NEW TRENDS IN THE TREATMENT OF OBESITY; THE ROLE OF PHYSICAL MEDICINE. A. P. CAWADIAS, Brit. J. Phys. Med. **6**:2 (Jan.-Feb.) 1943.

Any physical measure for reduction of weight is considered an adjunct to regulation of the diet. Exercise is useful only when applied with regard to its action on the nervous system, and not when it is intended simply to burn fat. The complicated movements executed by many obese persons and the wearisome Swedish exercises are of no avail; the same can be said of unrestricted golf and other games. It is a fact that many obese patients lose weight not when pushed to violent exercise but after being put to bed to rest. Exercise must be regulated with the object of arousing a sense of well-being. Respiratory exercises are important. There are limited indications for massage; it is useful as a postreduction treatment, since it enables the skin to adapt itself to the altered tissue mass.

Ultraviolet therapy has been thought to accelerate the action of reducing treatment. Electrotherapy was once used on the theory that it allowed the patient to burn his fat without fatigue, but this method has been more or less abandoned. Hydrotherapy using mild or moderate changes in temperature is advantageous. Turkish or peat baths of high temperatures are definitely contraindicated. Some mineral waters, because of their mildly laxative effects, are useful to constipated patients.

HARTMAN, Portsmouth, Va.

STAPHYLOCOCCUS AUREUS IN THE MILK OF NURSING MOTHERS AND THE ALIMENTARY CANAL OF THEIR INFANTS. J. T. DUNCAN and JACQUELINE WALKER, J. Hyg. **42**:474 (Oct.) 1942.

In 1940 and 1941, more than 2,500 swabs of materials were taken from the intestines and throats of newborn infants, both sick and healthy, and from the milk of their mothers. In one hospital, in 82 groups (each a mother and her baby) Staphylococcus aureus was found in the milk in 92.7 per cent, in the baby's throat in 91.5 per cent and in the baby's rectum in 74.4 per cent of the cases. In another hospital (5 groups) the percentages were 80, 100 and 40 respectively. No bacteria were found in the colostrum. In milk from lactating mothers who were not nursing babies, only 21.4 per cent of the samples contained the coccus.

In all of 41 cases of "flushed breasts," Staph. aureus was cultivated from the milk. The same organism occurred in 1 case of abscess of the breast, in 3 cases of purulent conjunctivitis in infants and in 6 cases of "green, hurried stools" in babies, of whom 1 died. Three mothers with vaginal discharge, one with pyelitis and one with perineal abscess yielded Staph. aureus.

In general the organisms were cultivated from the babies' throats earlier than from the breast milk; the type of organism was identical from both sources.

JANNEY, Wauwatosa, Wis.

FAILING LACTATION. MARGARET ROBINSON, Lancet **1**: 66 (Jan. 16) 1943.

In the infant welfare center at Norris Green during 1938 and 1940, detailed notes on 1,100 consecutive instances of premature weaning (i. e., before the seventh month) were taken at the time of the failure to continue breast feeding.

The normal lactation cycle of women successfully feeding their infants is described as follows:

1. *Period of Filling.*—This lasts about ten to thirty minutes; during it the mother has a sense of increasing heaviness in her breasts, apparently due to increase in the fluid rather than in the solid part of the milk. The rate of filling is peculiar to each woman, and the breasts of some mothers do not begin to fill until the infant begins to suck.

2. *Period of Emptying.*—This lasts five to seven minutes. The breasts are emptied by a rhythmic pumping out of the milk at a rate of forty to sixty jets per minute.

A few women felt neither a pringling sensation nor any heaviness after the second week of lactation and yet had an adequate milk supply.

3. *Refractory Period.*—This lasts two and one-half to three hours. Folley states that estrogens increase the percentage of solids in the milk as well as inhibit secretion. They may also govern the length of the refractory period, during which it is possible that milk solids are manufactured, whereas fluid is secreted during the period of filling.

The following types of failure were observed:

1. Dry: a. Partial failure: Engel has shown that quantity of breast tissue present varies from woman to woman, a fact which may have some bearing on this type of inadequate lactation. If complementary bottle feedings were given, the low level of secretion often continued for the full nine months.

b. Complete failure: This is the most common type and is due to either sudden or gradual cessation of both the solid and the liquid part of the secretion. In this type of failure the controlling mechanism of the whole lactation cycle seemed to be at fault. Many women continued having milk for the first feeding in the morning and the last one at night for some time after secretion at other times had ceased.

That the amount of milk secreted is in inverse proportion to the amount of muscular exercise taken was observed in the women suffering from a gradual failure of lactation.

2. Wet: This type is characterized by a distressing lactorrhea of "blue water." The breasts cannot retain milk owing to excessive peristalsis. This type of failure is gradual but rarely occurs after the fourth month. It seems to indicate that the ductless glands which control the filling and emptying periods of the lactation cycle are overactive.

3. Solid: In this type of failure apparently the breast has power to manufacture the milk solids but cannot fill itself with fluid and pump out the milk.

4. Agalactia: Complete absence of lactation is rare.

The causes of about half of the failures of lactation are unknown, and those of some of the remaining failures are doubtful. They may be due to a break in any one of the links in the chain of ductless glands controlling lactation.

Where there was a gradual failure of milk secretion a definite relationship was observed to exist between muscular exercise and amount of milk secreted.

LANGMANN New York.

A REFLEX GOVERNING THE OUTFLOW OF MILK FROM THE BREAST. H. K. WALLER, Lancet **1**:69 (Jan. 16) 1943.

Of the various factors on which the maintenance of secretion of milk depends, it is claimed that one is a reflex expelling mechanism which governs the outflow from the breast and which for convenience is called the draft reflex. The widely held view that the infant extracts its food by force of suction thus needs to be modified to one which recognizes that normally the milk, to a large extent, is delivered to it by this mechanism.

The draft reflex, which is so characteristic a feature after feeding has been established, does not seem to come into effective operation when the breasts first begin active secretion. During the state of engorgement, when the breasts may contain enormous quantities of milk, even the strongest baby may be able to obtain virtually nothing.

It is extremely important to know what proportion of early failures in breast feeding come from intrinsic defects in the structure of the breast and the nipple, from faulty performance by the child and from some artefact in the management of the lying-in period at variance with physiologic requirements.

The early suppression of milk secretion is commonly associated with overloading of the breasts in the first weeks of lactation. This state of engorgement may involve frustration of the draft reflex.

LANGMANN New York.

INNOVATION IN FLUID DIET IN INFANCY. PEDRO RUEDA, Arch. de pediat. **14**:199 (March) 1942.

An infusion made from mate (Ilex paraguayensis) is useful as a fluid for treatment of hydration. The author uses 60 Gm. of mate in 1,000 cc. of boiling water; this is allowed to cool and is given by mouth. Mate is rich in vitamin C and in matein, which acts as a cardiac stimulant. The flavor is pleasant.

LOZOYA S., Mexico, Mexico.

THE MILK PROBLEM IN CHILE. A. SCROGGIE, Rev. chilena de pediat. **13**:863 (Oct.) 1942.

The production of fresh cow's milk and particularly its cost are serious problems in Chile.

In large metropolitan or urban areas the supply of fresh milk often becomes inadequate during certain periods of the year. The author advises the establishment of industrial plants in such areas which can provide condensed, dried or evaporated forms of milk when fresh milk cannot be obtained.

In view of the bad economic, sanitary and hygienic conditions which exist generally in Chile, the author advises boiling of cow's milk in preference to pasteurization and expresses a preference for the use of acidified cow's milk for use in the feeding of infants.

Pasteurization is safe only if the milk is produced under clean conditions. Such milk is expensive and can be afforded by only the well-to-do. Adequate refrigeration must be provided for pasteurized milk.

For the large majority of the population in Chile the solution of the problem of supply of milk consists in the use of processed milks. The life and the health of Chilean children depend on their use.

SCHLUTZ, Chicago.

THE MILK PROBLEM IN CHILE. J. SCHWARTZENBERG L. and A. STEEGER S., Rev. chilena de pediat. **13**: 869 (Oct.) 1942.

There is inadequate production and, as a result, inadequate consumption of cow's milk in Chile. This creates a major problem in the feeding of infants and children.

Legislation and regulation of the milk industry must be wise and far seeing and must protect the interests of both the consumers and the producers. Both of these groups must be educated in all aspects of the problem.

The practical management of milk sanitation is a problem for a technically trained personnel.

Experience has shown that the state does not function well as the immediate supervisor of this program. It should have the function of formulating a national plan for the increased production and consumption of milk. It should concern itself with furnishing adequate support to agriculturists, hygienists and persons dealing with the economic and social aspects of the problem, in order that the population can be guaranteed the provision of pure, healthful milk. If these measures cannot be carried out, the existing laws for the pasteurization of milk should be amended and adjusted to the present needs of the problem and should be made to conform with the postulates laid down by the Pan American Child Congress of 1942.

SCHLUTZ, Chicago.

Vitamins; Avitaminoses

THE USE OF VITAMINS IN CLINICAL NEUROLOGY. CHARLES D. ARING, Bull. New York Acad. Med. **19**:17 (Jan.) 1943.

Vitamin deficiency may result from an insufficient intake of vitamins or from a faulty utilization of the vitamins ingested, for such reasons as loss through diarrhea, poor absorption or demand for detoxification of poisonous substances. While all the vitamins have been studied in connection with neurologic problems and all of them yielded some positive results when given to animals and human beings, the only group which may actually be considered of real value in this field is the B complex. A list of the neuritides which respond favorably to this vitamin group is comprehensively discussed and illustrated by case reports.

JAHR, Omaha.

VITAMIN THERAPY TODAY. ISAAC H. JONES, Laryngoscope **52**:805 (Oct.) 1942.

Much has been learned about nutrition and the vitamins in recent years. The "embryonic approach" to vitamin therapy is important. It is based on the theory that each germ layer of the embryo requires certain specific vitamins for its proper development. After birth and throughout life the tissues derived from this germ layer still continue to demand the same vitamins. Hence valuable clues are given as to what vitamin or vitamins are needed in lesions of this or that tissue.

The author divides the information concerning vitamins into four headings: "reliable," "probable," "possible" and "improbable."

Some of the statements listed as "reliable" are the following: 1. Of all the vitamins, vitamin B complex is the most apt to be deficient in the usual diet. 2. Foods improperly cooked lose their vitamin content. 3. In a vitamin deficiency it is usually better to prescribe several vitamins than a single one. 4. Dry scaly skin of the external auditory canal may be due to lack of vitamin A. 5. Retrobulbar neuritis may be due to the lack of the vitamin B complex, especially B_1. 6. Transverse fissures of the mouth, eczema of the ear and allied conditions may be relieved by vitamin B_2. 7. For surgical patients with low prothrombin, vitamin K is of value.

Included under "probable" is the fact that vitamin B_1 may relieve fever blisters.

Among the things mentioned under "possible" are the following: 1. The mucosa of the nose and throat may be improved, and hence infection cut down, by vitamin A and, perhaps, vitamins B_1 and B_2. 2. Deafness of cochlear origin may be helped by the vitamin B complex. 3. Vitamin B_1 by its effect on the nerves may lessen tinnitis and strengthen the voice. 4. Epistaxis may be helped by vitamin C.

Histologic studies were made on rats with a moderately low intake of vitamin B complex. No significant changes appeared in the mucosa of the nose or throat, but in the organ of Corti definite degenerative changes were observed.

Although the "embryonic" theory of vitamins seems to be borne out well clinically, depriving pregnant animals of certain vitamins would prove it.

Following this article is one by Jones and Covell giving a comprehensive review of the literature on vitamins in 1941-1942.

HITSCHLER, Philadelphia. [ARCH. OTOLARYNG.]

ACTIVATION OF PRO-VITAMIN D_3 IN THE RAT. E. GEIGER and S. LASSEN, Proc. Soc. Exper. Biol. & Med. **52**:11 (Jan.) 1943.

Forty-two rats which had been maintained on a rachitogenic diet for twenty-one days were studied to determine the action of provitamin D_3 (7-dehydrocholesterol) on the healing of rickets. The studies revealed that this substance is not effective, given either by mouth or subcutaneously, unless it has been irradiated or the animals to which it is given receive ample radiation. The fact that irradiation of the animals alone does not cause healing of the rickets indicates that provitamin D_3 is not synthesized in mammals and that any which is present in mammalian tissues comes from previously ingested food. The oxidation of cholesterol in the course of the preparation of food may perhaps produce 7-dehydrocholesterol.

HANSEN, Minneapolis.

CONTROL OF PELLAGRA. W. DEKLEINE, South. M. J. **35**:992 (Nov.) 1942.

The author states that since 1928 the death rate from pellagra has decreased by almost 77 per cent.

The widespread use of brewers' yeast, the promotion of gardening, the introduction of nicotinic acid and the educational work related to these projects have been largely responsible for this reduction.

The federal food relief program introduced in 1933 has not materially influenced the death rate from pellagra, although it has no doubt helped to prevent serious problems of malnutrition, particularly in chidren.

Nicotinic acid became available to the medical profession during the latter part of 1938 and has contributed materially to a lower mortality from pellagra since that time. It cannot, however, be distributed freely as such by public health agencies for use by the masses, as can be done safely with brewers' yeast. It can only be prescribed by physicians on an individual case basis.

Cases of advanced pellagra are far less common than they were a few years ago, although milder forms and subclinical types of the disease are still common. The problem cannot be brought under complete control until an adequate diet is within the reach of all potential victims of this malady.

SCHLUTZ, Chicago.

SLIT LAMP MICROSCOPE IN NUTRITION SURVEYS. J. H. KODICEK and JOHN YUDKIN, Lancet **2**:753 (Dec. 26) 1942.

The eyes of 496 elementary school children were examined with the slit lamp microscope.

Corneal vascularization, taken as an actual invasion of the clear cornea with vessels from the limbus and said to be indicative of deficiency of riboflavin, was found in about 4 per cent of the children. The proportion was significantly higher in older than in younger children.

The importance of examining the epithelial layer of the conjunctiva is stressed.

The authors' observations have led them to classify the children on the basis of various findings in the epithelium into five groups. The first group contains those children whose conjunctival epithelium is perfectly smooth and transparent, while the other groups contain those showing varying degrees of wrinkling and opacity, representing increasing severity of change.

LANGMANN, New York.

RICKETS IN RIO DE JANEIRO: CASES OBSERVED IN ONE YEAR. MAGALHÃES CARVALHO, ODILON DE ANDRADE FILHO, PAULO FIORAVANTE, JORGE DECOURT and ANITA PEREIRA, J. pediat. **8**:19 (Jan.-Feb.) 1942.

Sixty-five cases of rickets were studied at the Instituto Nacional de Puericultura in one year. The amount of phosphorus in the plasma was below normal in 52 per cent of the cases and above normal in 12 per cent; in the remainder rickets was present with normal phosphorus. The values for phosphatase were high in 62.8 per cent; no relation was found between them and the concentrations of phosphorus. Forty-three of the patients were mulattoes, 9 were Negroes and 13 were of the white race. Vitamin shock was found to be the most efficient treatment.

LOZOYA S., Mexico, Mexico.

TREATMENT WITH MASSIVE DOSES OF VITAMIN D. GLORIA LOVELL, Rev. Soc. pediat. de Rosario **7**:19 (Jan.-April) 1942.

Lovell reports 5 cases of rickets treated with massive doses of vitamins D and D_2 either orally or intramuscularly. She obtained considerably better results with this method than with the use of small repeated doses of vitamin D but she suggests subsequent treatment with small doses of vitamin D for some time. One of the cases seems to be of a type of rickets resistant to vitamin D. In no case were there symptoms of intolerance.

LOZOYA S., Mexico, Mexico.

Newborn

THE ROLE OF COLON ORGANISMS AND THEIR TOXINS IN EPIDEMIC DIARRHEA OF THE NEWBORN INFANT. WALLACE B. MCCLURE, J. Pediat. **22**:60 (Jan.) 1943.

McClure describes epidemics of infectious diarrhea of the newborn occurring in the nurseries of four hospitals. Cultures of stools revealed the presence of hemolytic colon and paracolon bacilli in the majority of infants with diarrhea. These organisms when grown in milk and fed to cats produced vomiting and diarrhea. Hemolytic colon bacilli when grown in an atmosphere of 10 per cent carbon dioxide produced toxins which when injected intraperitoneally into cats caused vomiting and diarrhea and, in the more toxic strains, even produced death. These toxins, however, did not hemolyze rabbit or sheep blood cells. In the epidemics described, colon and paracolon organisms isolated from infants that died were the most toxic, while less toxic strains were found in infants with milder diarrhea. McClure found evidence of faulty technic in each nursery involved, with every chance for the contamination of food with colon organisms.

STETTENBENZ, Buffalo.

VITAMIN K IN HEMORRHAGIC DISEASE OF THE NEW BORN INFANT. C. E. SNELLING with the technical assistance of WINNIFRED NELSON, J. Pediat. **22**:77 (Jan.) 1943.

Menadione (2 methyl 1-4 naphthoquinone), a synthetic vitamin K analogue, given orally in oil in 5 mg. doses to mothers after the onset of labor (at least four hours before delivery) was found definitely to prevent extreme hypoprothrombinemia in the newborn infant.

In the treatment of hemorrhagic disease of newborn infants compounds with vitamin K activity given intravenously or intramuscularly are effective in lowering the prothrombin time. If the baby is seen early and the hemoglobin content is not low, vitamin K may be all that is necessary to stop the bleeding. However, if the concentration of hemoglobin is low, transfusion is indicated in addition to the administration of vitamin K.

STETTENBENZ, Buffalo.

HEMORRHAGIC DISEASE OF THE NEWBORN. ELIZABETH B. S. SCOBBIE, Arch. Dis. Childhood **17**:175 (Dec.) 1942.

Scobbie reports a study of 146 infants with neonatal hemorrhagic disease (spontaneous internal or external hemorrhage in the newborn infant in the absence of trauma, infection or other definite disease). A comparison, in small groups of cases, of the effects of treatment by subcutaneous or intramuscular injections of blood, by blood transfusions and by vitamin K therapy is made. Blood transfusions, in this study, seemed to give the best results. Vitamin K was next and subcutaneous or intramuscular injections of blood lowest in efficacy.

KELLY, Milwaukee.

VITAMIN K REQUIREMENTS OF THE NEWBORN. M. TOOHEY, Arch. Dis. Childhood **17**:187 (Dec.) 1942.

It can now be assumed that vitamin K is specific for the prevention and treatment of hemorrhagic disease of the newborn infant. In this investigation an attempt was made to determine the dose of an analogue of vitamin K which would prevent any fall in the prothrombin level, and also the time of administration which would give the full effect.

Estimations of prothrombin made on 100 infants showed that a definite hypoprothrombinemia occurred during the first week of life. Seven infants had a fairly severe prothrombin deficiency, but in no case was there any hemorrhagic manifestation. Menadione in doses of 20 mg. to the mother before delivery and 5 mg. to the infant, raised the level of prothrombin to almost that of adult controls. A single dose of 10 mg. to the infant was entirely effective in preventing any appreciable fall in the concentration of prothrombin. It was sufficient to administer the vitamin K analogue during labor to be effective, if it was given at least two hours before delivery.

KELLY, Milwaukee.

BLOOD SUGAR IN THE NEWBORN. B. BASU, Indian J. Pediat. **10**:1 (Jan.) 1943.

The author found the average value for blood sugar of newborn infants within the first hour after birth to be 69.09 mg. per hundred cubic centimeters and that of the mothers within fifteen minutes after delivery to be 85 mg. per hundred cubic centimeters.

GONCE, Madison, Wis.

ENCEPHALITIS FOLLOWING INCLUSION CONJUNCTIVITIS. F. BAMATTER, Confinia neurol. **4**:314, 1942.

Bamatter reports 3 cases of encephalitis occurring in association with inclusion conjunctivitis in newly born infants. There were associated inflammatory hydrocephalus and albuminocytologic dissociation in the cerebrospinal fluid. The author states that while it has not been proved that keratoconjunctivitis with inclusion bodies and encephalitis in such infants have a common etiologic factor, the associated clinical manifestations are striking. He believes that this variety of encephalitis constitutes a clinical entity which has not been hitherto described.

DEJONG, Ann Arbor, Mich.
[ARCH. NEUROL. & PSYCHIAT.]

DACTYLOSCOPY IN THE IDENTIFICATION OF NEWBORN INFANTS. EGAS MONIZ, Pediat. e puericult. **11**:3 (Sept.-Dec.) 1941.

The author presents a description of a new apparatus, of his invention, to reproduce dactylograms. He has used this method at the Maternidad Climério de Oliveira, where he has a systematic service for the identification of newborn infants.

LOZOYA S., Mexico, Mexico.

Acute Contagious Diseases

FRANCISCO XAVIER BALMIS AND THE INTRODUCTION OF VACCINATION TO LATIN AMERICA. S. F. COOK, Bull. Hist. Med. **11**:543, 1942; **12**:70, 1942.

On Nov. 30, 1803 the Balmis expedition left Spain for the purpose of bringing the new discovery of vaccination to Central and South America, to Mexico and to the Philippines. The expedition consisted, besides Balmis, of 4 phycians, 2 surgeons, 3 male nurses, a former rectress of a foundling asylum and 22 children from an orphan asylum. The latter were taken as "human reservoirs" for the vaccine; the problem of transport of vaccine was a serious one, because the various methods of sending vaccine dried on threads or between glass slides were most unreliable. After a short stop at the Canary Islands, where vaccination was introduced, the expedition arrived at Puerto Rico in February 1804. There Balmis found that vaccination had been introduced before his arrival, though he claimed it to be of the spurious kind and not to be a protection against smallpox. That vaccination had been established before his arrival Balmis found in various other places, a fact which irritated him greatly and caused considerable unpleasantness in his relation with the local government.

From Puerto Rico Balmis apparently went to the north coast of South America and stopped at Caracas in Venezuela, from which he sent part of the expedition to Peru, while he went to Habana, Cuba. Another subdivision went to Guatemala, whose president had requested vaccine from the king. From Habana Balmis went to Yucatan and Vera Cruz. The reason for the detour to Yucatan, which was not in the original plan, is not clear. In both places he found vaccination already introduced, apparently from different sources. The independent expedition of Don Miguel José Monzón and his vaccinations in Campeche are carefully described, as well as Balmis' reactions, which often were most undiplomatic. From Vera Cruz the expedition went to Mexico, Mexico, for its most important phase. Much work awaited him there aside from the vaccinations—spread of propaganda in the city of Mexico as well as through the entire New Spain and care for the children who had come from Spain, a duty which had been emphasized in the royal orders.

Balmis' work in the city of Mexico was not easy; vaccination had been introduced into some suburbs, and the inhabitants of the city showed marked reluctance or indifference. Balmis had "to resort to force to obtain 12 children . . . for the purpose of insuring continuance of the precious vaccine," as he wrote himself to the viceroy. As it was his purpose not only to vaccinate a fair part of the population but to establish vaccination on a perpetual basis, he worked out a plan in two long documents: "Means for the Maintenance and Perpetuation of the Precious Vaccine in This, the Capital of Mexico" and "On the Establishment of a Public Vaccination Clinic."

A number of subsidiary expeditions to various Mexican cities during the winter of 1804 and 1805 are described in detail, with the approximate number of vaccinations, the way the expedition was received and the establishment of local vaccination boards. In a space of six months Balmis himself or his assistants visited every important town in Mexico, thousands of vaccinations were performed and the local medical men were trained in this practice. "The administration of smallpox prevention was vested in a series of local vaccination boards which . . . were under direct authority of the colonial government," and many free clinics were established.

The author attempts the difficult task of coming to a conclusion as to the number of people vaccinated from July 1804 to January 1806; his guess is that "100,000 might not be an overestimate," or about 2 per cent of the population; this figure does not seem quite so insignificant if one considers that large sections of the country were not visited, that vaccinations were confined to children, that the majority of the people over 20 years of age had had smallpox in the tremendous epidemics of 1779 and 1797 and that therefore only about 20 per cent of the people were not immune. The expedition may have reached about 20 per cent of the group just named.

The expedition finally went with 26 carriers to the Philippines, where Balmis separated from it; he went to Canton and thence to Lisbon and Madrid.

Much consideration is given the various introductions of vaccination before Balmis arrived and the possibility of intentional sabotage by local authorities for the purpose of gaining glory for themselves or for other reasons.

Most of the material is taken from the voluminous correspondence in the National Archives in Mexico City. The "Royal Orders: on the Propagation and Inoculation of Vaccine, etc." of Sept. 1, 1803, as well as Balmis' two documents on perpetuation of the vaccine and public vaccine clinics are reprinted in two appendixes.

The author has worked up an enormous amount of material in order to give a clear picture of this royal expedition, which lasted over three years.

ROSENTHAL, St. Paul.

PERTUSSIS TOXIN. MERRITT E. ROBERTS and ANNE G. OSPECK, J. Infect. Dis. **71**:264 (Nov.-Dec.) 1942.

Cultures of pertussis organisms grown in broth under suitable conditions produce a soluble toxic substance. The strength of this toxic substance can be increased by selection of culture.

This toxic substance is thermolabile, is lethal in animals, produces necrosis in rabbits and other animals and can be detoxified by a solution of formaldehyde.

The original toxic substance and that detoxified by solution of formaldehyde are both antigenic in rabbits, as shown by their ability to produce a neutralizing antibody. This neutralizing antitoxin can be demonstrated in vitro and in vivo.

TOOMEY, Cleveland. [AUTHORS' SUMMARY]

THE MECHANISM OF THE KENNY METHOD AND ITS CORRELATION WITH VITAMIN B THERAPY IN POLIOMYELITIS. W. J. MCCORMICK, M. Rec. **155**:525 (Dec.) 1942.

The author suggests the possibility of vitamin B_1 deficiency as an etiologic factor in anterior poliomyelitis, since there is considerable resemblance between the symptoms and pathologic changes of beriberi and those of poliomyelitis. Four cases which were diagnosed as instances of poliomyelitis are briefly reviewed. Large

doses of thiamine hydrochloride given hypodermically produced remarkable results.

FERDINAND, Peoria, Ill.

INFANTILE PARALYSIS. SISTER ELIZABETH KENNY, New York State J. Med. **42**:1645 (Sept. 1) 1942.

The terms used in the Kenny treatment are explained, and articles are quoted to show that excellent results have been obtained in the various places where this method of treatment has been used.

In the discussion, Boines of Wilmington, Del., and Daly of New York report excellent results from similar treatment. Boines also states that the statistics mentioned in the paper would tend to show that treatment of this muscle condition has brought the total recoveries from 20 to 80 per cent and that this proves that the damage in the cord is only one-fourth the damage in the muscle.

JOHN AIKMAN, Rochester, N. Y.

THE ROLE OF ORTHOPAEDIC APPLIANCES IN THE TREATMENT OF INFANTILE PARALYSIS. HENRY H. HORDAN, New York State J. Med. **42**:1651 (Sept. 1) 1942.

The ideal brace should be of the lightest weight consistent with durability. Correct fitting of the brace is also of great importance both for comfort and for treatment and from the economical point of view. While it is possible to supply standard splints for the acute stages of the disease, it is extremely difficult to adopt standard splints in the chronic stage. Braces must be designed, constructed and fitted for the requirements of each individual patient. Mass production does not give the desired results.

JOHN AIKMAN, Rochester, N. Y.

SKIN MANIFESTATIONS OF MENINGOCOCCAL INFECTION. G. B. MITCHELL-HEGGS, Brit. J. Dermat. **54**:283 (Nov.) 1942.

The author divides the cutaneous manifestations of meningococcic infection into those that occur during the acute infection and those that occur during the chronic infection. The eruptions occurring in the acute fever are:

1. Small evanescent rose pink or red macules or papules occurring on the first or second day of the disease. Urticaria may occur.

2. Petechiae, occurring in the mouth, frequently encountered after a few days of the infection.

3. Purpura and ecchymoses.

4. Herpes labialis, generally appearing on the second or third day, and herpes zoster, usually on the fifth day.

5. Serum rashes, which occur on the ninth to the twenty-first day.

6. Eruptions due to sulfonamide compounds usually appearing on the eighth day of administration. They may be either macular and morbiliform or associated with a number of scattered small papules.

The cutaneous lesions in the chronic infection are distributed in much the same way as in the acute fever: on the extensor aspect of the limbs, on the back and at points of pressure. There is often a generalized patchy erythema, which may be a manifestation of the circulating toxin; it is frequently stippled with petechiae, which can be detected by diascopy and have been shown to be due to emboli. These areas vary in diameter from 1 to 3 cm. and may be unassociated with petechiae or swelling. Nodular lesions, which are usually tender and suggest erythema multiforme in some cases and erythema nodosum in others, may appear on the legs. Purpura may be present.

Mitchell-Heggs stresses the importance of a complement fixation test of the blood as a diagnostic measure, in view of the difficulty of blood culture in certain cases.

BLUEFARB, Chicago. [ARCH. DERMAT. & SYPH.]

THE TREATMENT OF CEREBRO-SPINAL FEVER BY SULPHAPYRIDINE. ALEXANDER JOE, Edinburgh M. J. **49**:628 (Oct.) 1942.

In speaking of the administration of this drug the author stated that when doses are well tolerated the use of the largest amount that can be given is advisable, especially in the treatment of children under 5 years of age, in whom he has found the case fatality high. To children over 12 years he gave a preliminary intravenous injection of 2 Gm. of the soluble salt; to children under 12 years, 1 Gm. This was followed by oral doses every two hours for forty-eight hours and every four hours thereafter for two days. The drug is then administered three times a day as long as chemotherapy is necessary.

In tables the author compares the fatality for the various age groups when serum alone was used and since chemotherapy has been used. The mortality has dropped from 68.7 per cent with serum treatment to 18 per cent with sulfapyridine therapy. Arthritis was found to be a complication in 4 per cent of the cases in which sulfapyridine was used, and neuritis, the next most common complication, occurred in 1.8 per cent of these cases. Rashes were relatively common (7 per cent of the cases); urinary complications occurred in 4 patients, all boys. Case fatality rates are summarized as to the day of the disease on which chemotherapy was begun.

NEFF, Kansas City, Mo.

SCARLATINAL ENCEPHALOMYELITIS. N. W. WINKELMAN, J. Neuropath. & Exper. Neurol. **1**:363 (Oct.) 1942.

Because encephalomyelitis following scarlet fever is considered rare, Winkelman reports the clinical and pathologic observations in a case which appears unique in the severity of its neuropathologic changes. A 9 year old Negro girl manifested cerebral symptoms seven days after the onset of scarlatina. Competent staff members, who had treated many Negro patients with contagious diseases, stated that the rash was typical of that associated with scarlet fever. In addition to nuchal rigidity, the patient showed clinical evidence of widespread involvement of the cerebrum, brain stem and spinal cord. The cerebrospinal fluid contained 150 to 280 cells per cubic millimeter, over 90 per cent being lymphocytes. The patient became increasingly stuporous, pulmonary edema developed, and she died ten days after the onset of the illness.

Grossly, the brain showed extreme congestion and some edema but no softenings or hemorrhages. Microscopic examination revealed dilatation of the subarachnoid space, in which were congested blood vessels, some free blood and numerous histiocytes containing pigment and debris. Practically all the cortical nerve cells displayed extreme changes, ranging from ischemia to complete destruction. A few rod cells were present. There was notable increase in glia cells, the predominating form being the fibrillary astrocyte. The cytoarchitecture of the cortex was not greatly disturbed.

Both the gray and the white matter throughout the cerebrum, the brain stem and the spinal cord showed diffuse inflammatory involvement. Practically every small blood vessel was prominent because of swelling and proliferation of the endothelium, dilatation and

congestion or perivascular infiltration with lymphocytes and plasma cells, such areas being frequently surrounded by microglia cells. This infiltrative process was most prominent in the subcortex, in which perivenous necrosis was conspicuous. Many of the veins contained coagulated blood, and in a few fibrin formation was beginning. In the brain stem the same general vascular and glial reactions were present, the process being more intense in the white matter. The spinal cord showed extensive demyelination, notable loss of ventral horn cells, glial overgrowth and blood vessels "heavily mantled with lymphocytes, plasma cells, phagocytes and microglia."

The author emphasizes that in this case "the clinical condition was totally different from the usual mild recoverable neurologic complications seen infrequently in scarlet fever," which complications have been thought to be due to the toxins of the streptococcus. He concludes that "the central nervous complications were not the result of the 'scarlatinal organism itself,' but developed from the release by the streptococcus of a virus lying dormant within the central nervous system."

CAMPBELL, Philadelphia.
[ARCH. NEUROL. & SYPH.]

DIPHTHERIA IMMUNIZATION IN ENGLAND AND WALES. Lancet **2**:642 (Nov. 28) 1942.

According to the estimate of the Ministry of Health the proportion of children immunized in England and Wales is at least a third of the total number. Since, however, the child population will not be adequately protected against diphtheria, in the official view, until at least 3 of every 4 children are immunized, it is obvious that the response by parents to the scheme of immunization has far from reached expectations.

This article outlines some of the recommendations for propaganda.

LANGMAN, New York.

NOTES ON THE BACTERIOLOGY AND EPIDEMIOLOGY OF DIPHTHERIA IN BRAZIL: VACCINATION. ALCEU MARIZ, J. de pediat. **8**:395 (Sept.-Oct.) 1942.

The bacteriology, epidemiology and malignancy of diphtheria in Brazil are compared with those reported for some other countries, and the progress in vaccination against the same disease is reported.

LOZOYA S., Mexico, Mexico.

PROPHYLAXIS AND TREATMENT OF EPIDEMIC CEREBRAL MENINGITIS. A. ARIZTIA, Rev. chilena de pediat. **13**:853 (Oct.) 1942.

The present day treatment of cerebral meningitis consists principally in the prompt and early use of chemotherapy. All of the sulfonamide compounds are useful, but the best and most striking results have been obtained with sulfapyridine, sulfathiazole and sulfadiazine.

The dosage usually given was 0.2 to 0.3 Gm. per kilogram of body weight for the first forty-eight hours. The author preferably used sulfathiazole. The daily dose was divided into four parts, one being given every four hours. For the ensuing five days a dose of 0.1 to 0.15 Gm. per kilogram of body weight was given, and this was followed by a maintenance dose of 0.05 to 0.1 Gm. per kilogram of body weight up to the tenth or twelfth day of the disease.

The drugs were generally given by the oral route. If there was much vomiting or deep coma the drugs were given in soluble preparations by the intramuscular or intravenous route. The drugs were dissolved in isotonic solution of sodium chloride and given in the dosage of 1 Gm. two or three times in twenty-four hours. None of the preparations were given intraspinally. The author believes that they have little effect given by that route and that in the case of sulfapyridine such a method is dangerous on account of the possibility of the development of necrosis. Spinal punctures were done at the beginning of the attack, on the third day and one on the tenth day. Levels of the drug in the blood were taken at frequent intervals.

This form of treatment is not altered even in the face of the development of complications.

In the septic or fulminating forms of cerebral meningitis, the author advises the use of adrenal cortex extract along with massive dosage of the sulfonamide compounds. In cases of severe infections he advises the use of blood transfusions. The author does not use serum therapy except in those cases in which the patient shows an absolute intolerance to all sulfonamide compounds.

SCHLUTZ, Chicago.

DIPHTHERIA IN THE YEAR 1941. ELIAS FERRANDO and FELISA CARBONARI, Rev. Soc. pediat. de la Plata **3**:249 (Nov.) 1942.

In the province of Buenos Aires, diphtheria began to reach epidemic proportions in 1941; in that year there were 315 cases, whereas in 1940 the number was 105; in 1939, 97; in 1938, 56, and in 1927, 73. The age distribution in 1941 was: under 3 years, 50 cases; 3 to 6 years, 85; 7 to 10 years, 106; 11 to 14 years, 61, and over 15 years, 15. One hundred and sixty-two patients were male, and 155 were female. In 92 cases the disease was classified as mild, in 80 as severe (1 fatality), in 70 as submalignant (3 fatalities), in 34 as malignant (17 fatalities), in 21 as croupous (12 fatalities) and in 4 as nasal (1 fatality). The use of large doses of antitoxin did not decrease the fatality rate. At the end of the first week of illness, 87 per cent of the patients had a negative reaction to a Schick test, while in a smaller number of observations only 39 per cent had a negative reaction at the end of six weeks.

Considerable data were available as to previous immunizations and Schick tests of the patients. Of the total number of patients, 63 had previously been immunized, 183 had not been immunized and no information was available for 69; of the fatal cases (34) the numbers were 4, 22 and 8 respectively. Twenty-eight per cent of the successfully immunized patients (those found to have a negative Schick reaction after immunization) had the malignant or submalignant type of the disease, while the percentage for the total immunized was 35 and for the nonimmunized 33.

HIGGINS, Boston.

Acute Infectious Diseases

THE COMPARATIVE THERAPEUTIC ACTIVITY OF SULFONAMIDES AGAINST BACTERIAL INFECTIONS IN MICE. E. K. MARSHALL JR., J. T. LITCHFIELD JR., H. J. WHITE, A. C. BRATTON and R. G. SHEPHERD, J. Pharmacol. & Exper. Therap. **76**:226 (Nov.) 1942.

The therapeutic activity of thirty-three typical derivatives of sulfanilamide against a streptococcic infection in mice has been compared. With the exception of sulfapyridine none of these derivatives was found to be significantly more active than sulfanilamide, while most of them were less active than the parent compound. On a pneumococcic infection, sulfapyridine, sulfathiazole, sulfadiazine, sulfamethyldiazine, sulfapyrazine and sulfaguanidine are all more active than sulfanilamide. There appears to be a definite specificity in the action of

sulfanilamide derivatives on bacterial infections in mice. Although all compounds which were active in vivo were also active in vitro, there appears to be no quantitative relation between in vitro and in vivo activity.

AUTHORS' SUMMARY.

EPIDEMIOLOGIC ASPECTS AND LABORATORY DIAGNOSIS OF SALMONELLA INFECTIONS. S. BORNSTEIN, New York State J. Med. **42**:2215 (Dec. 1) 1942.

The New York Salmonella Center was established in the department of bacteriology at the Beth Israel Hospital three years ago. Of 2,000 cultures received for identification and typing, 657 were of Salmonella. Of 34 fatal cases reported to the center, only 3 were due to paratyphoid bacilli. The most dangerous salmonella infection was the septic type, which accounted for three-fourths of the deaths.

Salmonella infections were observed in the newborn, and the disease as it occurred in one nursery was similar to epidemic diarrhea of the newborn.

Methods of identification are discussed. Antigenic analysis is the only reliable way of classifying bacteria of the salmonella group, though agglutination tests are of some value.

AIKMAN, Rochester, N. Y.

BACILLARY DYSENTERY. NELLES SILVERTHORNE and AGNES WALKER, Arch. Dis. Childhood **17**:210 (Dec.) 1942.

This report deals with 29 infants and children with bacteriologically proved dysentery. The main symptoms were fever (28), diarrhea (22), vomiting (13), blood in the stools (7), drowsiness (7), convulsions (5) and abdominal pain (5). The patients were treated, in the main, with fluids and with a mixture containing bismuth and camphorated tincture of opium with chalk. Seriously sick patients received intravenous injections of dextrose solution, and some received blood transfusions. All patients recovered rapidly as a result of the administration of fluids.

In 23 of the 29 patients who were suffering from dysentery, the infecting organism was Bacillus dysenteriae Sonne, in 3 Bacillus dysenteriae Flexner W, in 1 Bacillus dysenteriae Flexner Y and in 2 Bacillus dysenteriae Newcastle.

KELLY, Milwaukee.

THE INFLUENCE OF SOCIAL CONDITIONS UPON DIPHTHERIA, MEASLES, TUBERCULOSIS AND WHOOPING COUGH IN EARLY CHILDHOOD IN LONDON. G. PAYLING WRIGHT and HELEN PAYLING WRIGHT, J. Hyg. **42**:30 (Oct.) 1942.

Deaths among London children up to 4 years of age are listed for diphtheria, measles, tuberculosis, pertussis, bronchitis and pneumonia, from 1931 to 1938 inclusively. The deaths from pneumonia for the eight year period—some 48,000—totaled about six times those from the first four diseases (pertussis and measles leading among these). Statistical evidence indicates that many deaths attributed to pneumonia and bronchitis should be attributed to one of these specific diseases, often the primary illness.

A correlation exists between the incidence of diphtheria and the size of the family. The infection is transmitted from the school child to younger brothers and sisters more readily under inferior housing conditions.

The primary attacks of measles are usually those in children of school age, those in younger children being secondary. Halliday found measles much more severe in overcrowded districts, as did the author. This is partly because the average age of acquiring it is earlier in these districts.

Tuberculosis among children is acquired mostly from adults of the family, and the bovine type, in decreasing numbers, from milk. Tuberculosis too is more frequent in crowded districts.

Transmission of pertussis is strongly associated with overcrowding, but the size of the individual family has little influence.

JANNEY, Wauwatosa, Wis.

JUVENILE RHEUMATISM: ITS PROBLEMS. REGINALD MILLER, Lancet **2**:563 (Nov. 14) 1942.

"We may look for evidence of chorea in cases of rheumatism rather than for rheumatism in cases of chorea." The dictum, attributed to Sir Thomas Barlow, that "all rheumatic children show chorea, only some more so" is strictly true.

To accept the hypothesis of streptococcic causation as true does not imply that it has yet been proved to express the whole truth, although there are not lacking signs that ultimately it will attain even to this position. Three general considerations favor this hope: it has lived for over forty years; not only is it without competitors, but it has formed and still forms the basis of nearly all laboratory research on acute rheumatism; and the younger generation of physicians, unmindful of past controversies, accept juvenile rheumatism without difficulty as a streptococcic disease and allow this view to influence their treatment.

"The closeness of the relationship between tonsillar infection and juvenile rheumatism in all its phases can hardly be overemphasized. The figures obtained at the Paddington Green Children's Hospital demonstrated that 89 per cent of rheumatic children showed infected tonsils and that the chance of spontaneous cure was well under 5 per cent. Thus the call for the removal of diseased tonsils can hardly be questioned on theoretical grounds. In practice the value of this procedure is shown not so much by the prevention of further attacks of rheumatism as by the modified severity of the infection, so that the danger to the heart is reduced; indeed it may be claimed that it is exceptional for permanent heart disease to develop for the first time in a tonsillectomized child."

LANGMANN, New York.

INVESTIGATIONS OF AN INFLUENZA EPIDEMIC IN MILITARY CAMP IN VICTORIA, MAY 1942. F. M. BURNET, W. I. B. BEVERIDGE, DIANA R. BULL and E. CLARK, M. J. Australia **2**:371 (Oct. 24) 1942.

An account is given of the clinical and epidemiologic features of a typical epidemic of influenza A observed in a military camp in Victoria, Australia, during May 1942. By means of the method of amniotic inoculation of chick embryos virus was isolated from 8 of 10 throat washings obtained from patients with influenza in typical form in the first two days of illness. Samples of serum obtained during the acute stage and during convalescence showed a sharp rise in antibody (by the Hirst red cell agglutination technic) against the current strain. Comparison with results of determinations on an unselected camp population confirmed the general finding that susceptibility to influenza is significantly correlated with low initial level of antibody, but that a relatively high level of antibody in a person is no guarantee of his insusceptibility. All primary isolations produced fluids with a higher titer against guinea pig cells than against cells from fowls, but sometimes after a single passage and always after three or four the normal equality of titer was gained.

GONCE JR., Madison, Wis.

CEREBELLAR SYNDROME OF MALARIAL ORIGIN. MARIO MENDEZ and NOE HUAMAN, Rev. de neuro-psiquiat. **4**:106 (March) 1941.

A child aged 13 years was stricken with malarial fever, with chills, headache, fever and vomiting. Two months later, he felt dizzy and had difficulty in articulating, and his movements became incoordinate. He was unable to stand or walk without help, although muscular power and sensation were unaffected. There were also dysmetria, dysdiadokokinesis and nystagmus.

Three months after the onset of the illness Plasmodium vivax was found in the blood. With the administration of specific treatment (presumably quinine) the fever was abolished, and there was regression of the cerebellar syndrome during the following fortnight.

DE GUTIÉRREZ-MAHONEY, Coral Gables, Fla.
[ARCH. NEUROL. & PSYCHIAT.]

MESTER'S TEST IN THE DIAGNOSIS OF RHEUMATIC DISEASE OF CHILDREN. J. F. MORANO BRANDI and A. A. DATO, Rev. Soc. pediat. de la Plata **3**:233 (Nov.) 1942.

Mester's test consists in the making of white cell counts of blood taken from the finger before and one-half and one hour after intradermal injection of 1 cc. of 0.1 per cent salicylic acid on the forearm (five injections of 0.2 cc. each). If the leukocyte count falls less than 15 per cent after the injection, the result of the test is negative, while if it falls more than 15 per cent, it is positive. The subject should not have recently received sodium salicylate therapeutically.

In the authors' study, 34 children with rheumatism were tested; 30 were found to give a positive reaction on the first trial and 2 more on the second trial; thus 94.2 per cent of children who themselves had rheumatism or whose parents had it showed positive reactions. Of tests on 23 children with no personal or familial history of rheumatism, 19 had negative and 4 positive reactions.

HIGGINS, Boston.

Chronic Infectious Diseases

BRONCHIAL OBSTRUCTION AND PULMONARY ATELECTASIS. EDWARD M. KENT, Am. Rev. Tuberc. **46**:524 (Nov.) 1942.

Two general types of bronchial obstruction are recognized as occurring during the course of childhood tuberculosis, one the result of intrinsic tuberculosis within the wall of the bronchus and the other the result of compression from without due to increase in size of adjacent lymph nodes. In this study the principal objective was to determine whether bronchiectasis could be shown to be a sequel of pulmonary atelectasis occurring during the course of childhood tuberculosis, and further to add evidence to the contention that so-called epituberculous pneumonia is in reality pulmonary atelectasis. In the 10 cases of atelectasis reported, 7 patients had bronchiectatic changes undoubtedly secondary to bronchial obstruction. The universal factors determining the production of secondary bronchiectasis are the duration of the bronchial obstruction and the severity of the infection set up in the pulmonary segment. In this small group of cases, not one of the children showed symptoms of bronchietatic infection. The duration of the obstruction, however, appeared to be of prime importance, since in general when the obstruction lasted less than six months bronchiectasis did not result. The absence of residual bronchial stenosis of any appreciable degree supports the contention that the bronchial obstruction was due to an external compression rather than to intrinsic bronchial disease. Of the 8 cases of lobar atelectasis, the condition ultimately became arrested in 7, while in 2 patients with atelectasis of an entire lung resolution was not complete. Kent believes that these cases furnish further evidence in support of the belief that epituberculous pneumonia is in reality atelectasis resulting from occlusion of a bronchus. The prognosis of this syndrome appears to be favorable.

EUGENE SMITH, Ogden, Utah.

TUBERCULIN SENSITIVITY IN CHILDREN WITH BONE TUBERCULOSIS. PHILLIP J. HOWARD, JOSEPH A. JOHNSON and C. LESLIE MITCHELL, Am. Rev. Tuberc. **46**:532 (Nov.) 1942.

Since tuberculosis of bone has usually been preceded by a primary infection in a lung or a hilar lymph node, the relation of allergy to this condition presents a problem of some complexity. Lesions of bone have a tendency to be multiple, because they are metastatic and because children suffering from these conditions have been through a stage of blood-borne infection. For these reasons the exact amount of old tuberculin causing the first reaction is quite variable. Lower levels of sensitivity are characteristic of the early stages of the disease, and a positive reaction may appear even before any roentgenographic sign of destruction of bone is evident. However, a rise to a high level of sensitivity as the disease develops and a subsequent fall as healing progresses are characteristic features of osseous tuberculosis. Extreme sensitivity does not indicate that the condition is serious or the prognosis poor unless the sensitivity fails to recede. Failure to recede over a period of three years indicates active infection, spread of the disease and a poor prognosis.

EUGENE SMITH, Ogden, Utah.

HEMIPLEGIA IN TUBERCULOUS MENINGITIS. CLARENCE W. OLSEN and ALBERT F.* BROWN, Bull. Los Angeles Neurol. Soc. **7**:189 (Dec.) 1942.

Olsen and Brown report 4 cases of hemiplegia associated with tuberculous meningitis. The incidence of this complication in a series of 378 cases of tuberculous meningitis with both clinical and postmortem reports slightly exceeded 10 per cent.

LESKO,, Bridgeport, Conn.
[ARCH. NEUROL. & PSYCHIAT.]

CONGENITAL TUBERCULOSIS. GREGORY L. ROBILLARD, New York State J. Med. **42**:1955 (Oct. 15) 1942.

A case of congenital tuberculosis in an infant born two months prematurely is reported. Postmortem examination revealed a widely disseminated blood-borne infection which had reached the fetus through the umbilical vein.

AIKMAN, Rochester, N. Y.

TUBERCULOSIS IN ADOLESCENTS AND YOUNG ADULTS. RALPH HORTON, New York State J. Med. **42**:2131 (Nov. 15) 1942.

A study was made of 100 cases of tuberculosis in patients between 15 and 24 years of age. With early diagnosis and prompt treatment development of the disease was arrested in 72 per cent of the cases, in 20 per cent it remained quiescent or active and in 8 per cent the patient died. A plea is made for early diagnosis and treatment.

In the discussion, Johnson stated that at the Monroe County (N. Y.) Tuberculosis Sanatorium a patient was denied admission until persons exposed to infection from him had been given or had consented to have roentgen examinations. At the present time 73.5 per cent of all exposed persons are given such examinations.

AIKMAN, Rochester, N. Y.

Diseases of Blood, Heart and Blood Vessels and Spleen

PROTHROMBIN STUDIES: III. EFFECT OF VITAMIN K UPON HYPOPROTHROMBINEMIA INDUCED BY DICUMAROL [DICOUMARIN] IN MAN. SHEPARD SHAPIRO, MILTON H. REDISH and HAROLD A. CAMPBELL, Proc. Soc. Exper. Biol. & Med. **52**:12 (Jan.) 1943.

Study of 8 human subjects indicated that synthetic vitamin K in relatively large amounts prevented the prolongation of the prothrombin time of diluted plasma produced by the oral administration of 50 mg., the smallest effectual dose, of dicoumarin (3, 3′-methylenebis [4-hydroxycoumarin]).

HANSEN, Minneapolis.

A CASE OF ACHLORHYDRIC HYPOCHROMIC MICROCYTIC ANEMIA IN A CHILD OF EIGHT YEARS. JOHN V. DACIE and PHILIP ELLMAN, Brit. J. Child. Dis. **39**:97 (Oct.-Dec.) 1942.

In the case reported the diagnosis of achlorhydric hypochromic anemia was based on the initial blood picture, the persistent histamine-refractory achlorhydria, the absence of steatorrhea and the excellent response to large oral doses of iron with regression of the splenic enlargement.

Achlorhydria is frequently associated with hypochromic and other types of anemia in infancy and childhood.

LANGMANN, New York.

ANEMIA IN WOMEN AND CHILDREN ON WAR-TIME DIETS. LUCY WILLS, HELEN M. M. MACKAY, KAITILIN BINGHAM and R. H. DOBBS, J. Hyg. **42**:505 (Oct.) 1942.

During 1941 and 1942, hemoglobin estimations were made on 544 women and 530 children, and these were compared with prewar records for similar groups. For the women, the average dropped from 99 to 89.5 per cent. Of 364 children aged 6 months to 5 years, from clinics, welfare centers and residential nurseries, the average level was 75.4 per cent between 6 and 12 months of age, 72.8 per cent between 1 and 2 years and 81.8 per cent between 4 and 5 years. Older children (5 to 13 years) averaged 80.3 per cent, while the 15 year old group had 89.3 per cent and adolescent factory girls 98.7 per cent.

The readings among the younger groups were considered pathologically low, that of the 5 to 13 year old group being 10 per cent lower than in a similar group in 1935. Several factors may be responsible, but lack of iron seems the most important. The reduction seems significant enough to warrant further investigation and official action.

JANNEY, Wauwatosa, Wis.

UNUSUAL MANIFESTATION OF LYMPHATIC LEUKEMIA. B. P. TRIBEDI and S. K. BONERJEE, J. Indian M. A. **12**:139 (Feb.) 1943.

The authors report a case of acute lymphatic leukemia in which the first symptom was retention of urine. At the third catheterization, thirty-eight hours after the second occurrence of retention of urine, pure blood was recovered from the bladder. Death occurred sixty-five hours after the onset of symptoms. Postmortem examination revealed a large hematoma of the wall of the bladder.

GONCE, Madison, Wis.

A FATAL CASE OF TACHYCARDIA IN AN INFANT. E. GARCIA CARRILLO, Rev. argent. de cardiol. **9**:247 (Oct.) 1942.

A 3 month old child died, after a few hours' illness, of pulmonary edema. Tachycardia (214 beats per minute) was present, which clinically and electrocardiographically resembled the supraventricular paroxysmal type.

SANFORD, Chicago.

PANMYELOPHTHISIS (APLASTIC ANEMIA) IN A CHILD. E. G. CASELLI, Rev. Soc. pediat. de la Plata **3**:299 (Nov.) 1942.

A boy of 11 years had been declining in health for six months; he became anemic, had ecchymotic areas from minor trauma and had occasional spells of fever. The family history was irrelevant. His erythrocyte count was 950,000, and his leukocyte count 1,700, with 16 per cent granulocytes. The hemoglobin content of the blood was 18 per cent. Transfusions had no substantial effect. After having fever with a temperature of 39 to 40 C. (102 to 104 F.) for seven days, he went into coma and died. Autopsy was not performed. No etiologic explanation for the condition was apparent.

HIGGINS, Boston.

Diseases of Nose, Throat and Ear

THE TREATMENT OF CONGENITAL ATRESIA OF THE CHOANAE. V. H. KAZANJIAN, Ann. Otol., Rhin. & Laryng. **51**:704 (Sept.) 1942.

Developmentally, the primitive nasal pouch grows back to meet the ectoderm of the oral fossa. The membrane ruptures through on the thirty-fifth to the thirty-eighth day of fetal life. Lack of rupture is thought to be the cause of choanal atresia. Bone formation may occur in the occluding membrane, but atresia may remain membranous in whole or in part. It may be unilateral or bilateral. In cases in which it is bilateral there is constant mouth breathing, the palatal arch is usually high and there are dental irregularities. Frequently the nasopharynx shows dry, atrophic mucosa, with absence of adenoid tissue. In the cases of unilateral atresia symptoms are less pronounced, and the condition may be overlooked. The following points are helpful in making the diagnosis: (1) One or both sides of the nose are completely obstructed, with no other clearcut cause, such as septal deflection, foreign body or tumor; (2) the floor of the nose is covered with mucoid secretions; (3) a probe cannot be passed into the nasopharynx; (4) inspection or palpation of the posterior choanae presents a characteristic picture; (5) roentgenographic study with an opaque oil gives diagnostic evidence.

The author describes his operation, which consists of an incision made at the base of the columella and carried backward along the floor of the nose through the cartilaginous septum as far as the perpendicular plate of the ethmoid bone. Here the incision is carried up almost vertically to the roof of the nose. The cartilaginous septum can then be held aside while the bony septum is removed, together with the attached soft tissues, all the way back to the atresia. Usually a chisel is required to pierce the occlusion. A Kerrison forceps is used to remove the rest of the obstruction. The columella and the cartilaginous septum are then replaced and sutured in place, and the nose is packed with finger cot plugs for twenty-four hours. Three cases are reported.

MILLER, Philadelphia. [ARCH. OTOLARYNG.]

CHRONIC OTORRHEA DUE TO FOOD SENSITIVITY. LOUIS J. NOUN, J. Allergy **14**:82 (Nov.) 1942.

The author reports the cases of 2 boys with chronic otorrhea which was relieved by the removal of offending foods from the diet. He stresses the importance of thinking of sensitivity of the drum membrane and the middle ear in cases of chronic otorrhea in patients

with a family history of allergy when the recurrent attacks of discharge from the ears are featured by an absence of fever.

HOVER, Cincinnati.

A STUDY OF THE ONSET AND DEVELOPMENT OF STUTTERING. WENDELL JOHNSON, J. Speech Disorders **7**:251 (Sept.) 1942.

Forty-six stuttering children were compared with 46 nonstuttering children in regard to birth conditions, general developmental conditions, speech development, diseases and injuries, stuttering, handedness in the family background and handedness and eyedness of the group studied. No significant facts were disclosed. Johnson suggests that such stuttering in its serious forms develops only after a diagnosis of stuttering is made and as a consequence of the diagnosis.

PALMER, Wichita, Kan.

SILENT MASTOIDITIS. GEORGE D. WOLF, New York State J. Med. **42**:1755 (Sept. 15) 1942.

Cases of mastoiditis in which few if any symptoms are apparent are often overlooked by pediatricians. The use of the sulfonamide drugs tends to mask symptoms even more. Case histories of 5 children are given to prove these points. In 2 of these children, postauricular swelling first disclosed the disease. In an 11 month old infant, transient paralysis of the facial nerve disappeared after operation. The other 2 children were operated on because of long-continued drainage from the ear.

AIKMAN, Rochester, N. Y.

BRONCHOGRAPHY IN CHILDREN. C. ELAINE FIELD, Lancet **2**:357 (Sept. 26) 1942.

A new technic of bronchography of children is described in which they are anesthetized with nitrous oxide, while a special intratracheal needle is introduced through the cricothyroid membrane. During the injection of the iodized oil no anesthetic is administered, since the best bronchograms are obtained when the patient is fully conscious.

This method is suitable for children 5 years of age and over. For infants under 5 years the less satisfactory method with open ether anesthesia is used.

LANGMANN, New York.

STAPHYLOCOCCIC LARYNGOTRACHEOBRONCHITIS. ANT. LEÃO VELOSO and E. CORRÊA DE AZEVEDO, Arch. de pediat. **14**:469 (Sept.) 1942.

A case of acute laryngotracheobronchitis complicated with abscess of the lung is reported. The patient was treated first with antidiphtheritic serum, then with sulfanilamide, sulfathiazole, sulfapyridine and staphylococcic antitoxin and finally by tracheotomy and aspiration. Total recovery came after four months of treatment.

LOZOYA S., Mexico, Mexico.

Diseases of Lungs, Pleura and Mediastinum

SULFADIAZINE IN THE TREATMENT OF LOBAR PNEUMONIA. ABEL LEVITT and JOSEPH M. PRESANT, M. Rec. **155**:477 (Oct.) 1942.

Twenty-five patients with pneumonia treated with sulfadiazine are reported on, and the results are compared with those for a previous larger series of patients treated with sulfadiazine and sulfathiazole. It was observed in the small series that sulfadiazine produces similar reactions to the other sulfonamide drugs but that they are less pronounced. Five of this group of 25 patients had unresolved pneumonia for a number of weeks which finally cleared up. In these two groups of cases, sulfapyridine gave the best results, with the lowest mortality and with few complications. Sulfathiazole did not give as rapid a clinical response as sulfapyridine, and it produced similar reactions.

FERDINAND, Peoria, Ill.

THERAPEUTIC PROCEDURES IN BRONCHIAL ASTHMA. W. C. SPAIN, New York State J. Med. **42**:1631 (Sept. 1) 1942.

Since it is well established that allergic conditions are inherited, infants and children of an allergic family should be protected from the commoner inhalant and dietetic antigens. Dogs and cats should be banned from the household. Feather pillows, down, cotton and kapok bedding should be replaced. The excessive use of nuts and chocolate must be avoided, and children should not be coaxed to eat food that they instinctively dislike. Particularly, exposure to excitants identified by history or by cutaneous tests should be prevented. This principle of escape from the influence of home surroundings and diets is probably responsible for the development of many institutions and spas.

Various drugs used in the treatment of asthma are discussed. A 1:100 solution of epinephrine hydrochloride as a spray for inhalation, should be used with caution in children, since desquamation of the tracheal epithelium and loss of cilia may result. Theophylline alone or combined with ethylenediamine is especially useful in severe asthma. Morphine is especially dangerous, as it suppresses the respiratory center, abolishes the cough reflex and permits development of mucous obstruction. Patients may also become sensitive to morphine. Sulfadiazine may well be used to control infections of the respiratory tract, since such infections increase the mortality in bronchial asthma. Belladonna, calcium, histamine, histaminase and potassium chloride have not yet been proved of great value. The intratracheal injection of iodized oil is "of passing value" and not without danger.

Purgation, starvation and continuous rest in bed, the use of potassium and sodium iodide and other old time methods may be tried with advantage. Above all, proper climate is of advantage in treatment; Spain advises the high altitudes of the Southwest, particularly in Arizona and New Mexico.

AIKMAN, Rochester, N. Y.

VIRUS PNEUMONIA. S. S. RIVEN and E. A. STERN, South. M. J. **35**:976 (Nov.) 1942.

The authors state that virus pneumonia is a disease that has been only recently identified and is being recognized with increasing frequency.

Virus pneumonia is characterized by a gradual onset, generalized symptoms of variable severity, cough, fever, inconspicuous signs over the pulmonary fields, with frank roentgen evidence of pulmonary involvement, scant mucopurulent sputum, from which the common pathogenic organisms cannot be isolated, and a low white blood cell count.

The causation of the disease is not entirely understood, but it would seem probable from evidence to date that the disease is caused by a filtrable virus that has not been hitherto identified; it may possibly be due to a rickettsial organism.

SCHLUTZ, Chicago.

Nervous Diseases

THE PREVENTION AND TREATMENT OF CONVULSIVE DISORDERS. WILLIAM G. LENNOX, Bull. New York Acad. Med. **19**:47 (Jan.) 1943.

This paper deals with epilepsy as a convulsive disorder frequently receiving insufficient attention from the point of view of preventive treatment. Too often, the author states, the physician on finding a familial predisposition to epilepsy throws up his hands in despair and immediately concludes that epilepsy is certain to develop in the patient. Such an attitude obviously precludes any interest in prophylaxis. Actually the person with a familial history of the condition may, through proper guidance along sound principles of hygiene, delay indefinitely the action of the trigger mechanism essential to produce the seizures.

A note is also sounded on the guidance of the patient who is already subject to epilepsy. His physical, mental and social guidance will in the average case determine whether the patient will remain a burden to himself and his family or whether he will find ways and means of sustaining himself through employment at tasks in which so many epileptic persons can find happiness through creative achievement and useful occupation.

While some persons with epilepsy suffer from physical and mental deterioration, most of the men and the women having seizures are of average usefulness in a society in which work of all kinds is begging for man and woman power.

JAHR, Omaha.

OBSERVATIONS ON THE FUNCTIONAL DEVELOPMENT OF THE FETAL BRAIN. JOSEPH BARCROFT and DONALD H. BARRON, J. Comp. Neurol. **77**:431 (Oct.) 1942.

Barcroft and Barron studied the normal behavior of 200 sheep fetuses ranging in age from 32 to 147 days with special reference to respiratory movements and to righting and postural movements. Movements of the diaphragm and intercostal muscles were first observed in a fetus 38 days old. The respiratory movements pass through four phases of development: (1) a phase in which the diaphragm contracts with the muscles of the neck, and only with them; (2) a phase in which contractions of the diaphragm are dependent on muscular activity but are not linked to the activity of any specific group of muscles; (3) a phase in which the respirations outlast the stimulus or body activity, and (4) a phase of inhibition. Righting and postural efforts develop in the following order: tonic neck reflexes on the legs; head righting; compensatory movements of the eyes, and body righting. A study of these features was made in fetuses with lesions in the brain stem ranging from the upper cervical portion of the cord to the cerebral cortex. The operations were performed on fetuses between 40 and 70 days of age, and the postoperative study was made on fetuses between 54 and 132 days of age. The region of the brain responsible for the first two phases of respiration is in the lower portion of the medulla, that for the third phase in the pons and that for the fourth phase in the caudal half of the midbrain. The region responsible for the tonic neck reflexes on the legs is the upper cervical portion of the cord and the lower part of the medulla, and that for head righting is in the pons and the lower part of the midbrain. Compensatory movements of the eyes and body righting occur only if the brain stem behind the diencephalon and spinal cord is intact.

ADDISON, Philadelphia.
[ARCH. NEUROL. & PSYCHIAT.]

THE RELATION OF NEUROTROPIC STREPTOCOCCI TO ENCEPHALITIS AND ENCEPHALITIC VIRUS. E. C. ROSENOW, Proc. Staff Meet., Mayo Clin. **17**:551 (Nov. 4) 1942.

Rosenow has reported consistent isolation of a neurotropic type of streptococcus in epidemic encephalitis, epizootic encephalitis in the fox and equine encephalomyelitis. This type of streptococcus was isolated from fifty-five emulsions made from the brains of human beings, horses, sheep, a hog, a dog, a mink, a bat, chickens, wild ducks, a goose, a pheasant and fish that had died of encephalitis during the studies on the epidemic of encephalitis in North Dakota and Minnesota in 1941. The streptococcus was demonstrated in material obtained from nature, such as mosquitoes and flies; indoor and outdoor air; dust from air-conditioning filters; water from first rains, lakes, rivers and streams, and soil from the bottom of a lake where deep-feeding ducks were dying. These materials and old chick embryo cultures of these materials which contained the streptococcus were inoculated into guinea pigs and mice. Thirty-nine specimens were inoculated into 174 guinea pigs and 236 mice; 53 per cent of the guinea pigs and 40 per cent of the mice died of encephalitis. "The parallelism of isolation of this type of streptococcus from, and the occurrence of encephalitis after inoculation of, diverse materials, including washings from outdoor air, was so striking and constant as to suggest a relation between the streptococcus and the 'virus' and that the inciting agent of the epidemic, which occurred over such a vast area, was air borne. Accordingly, experiments were performed to test these ideas a step further."

"Pure cultures of forty-three different strains of the streptococcus, and filtrates of old chick embryo cultures of the streptococcus, far removed from original source and representing dilution of original material of never less than 10-20, were inoculated intracerebrally, intralingually or both intracerebrally and intralingually . . . into 126 guinea pigs and 307 mice. Forty-four per cent of the guinea pigs and 50 per cent of the mice [died of] encephalitis. Similar results were obtained in Rhesus monkeys.

"The virus was found in the brains of animals that had died of encephalitis after inoculation of emulsions from brain tissue (1) of animals and fowl that had succumbed to spontaneous encephalitis, (2) of animals that died of encephalitis after inoculation of material from nature and (3) of animals that succumbed after injection of virus derived from the streptococcus; this virus produced encephalitis consistently in guinea pigs and mice in from three to seven or more passages. The streptococcus was isolated after the first or second passage of the three types of material from the brains of animals that had succumbed to encephalitis as follows: from eighty (40 per cent) of 198 brains of guinea pigs cultured, from 163 (36 per cent) of 450 brains of mice cultured, and from the brains of animals that succumbed to successive passages of the virus. Eighty-nine guinea pigs and 243 mice remained well after inoculation of forty-seven control emulsions and filtrates of emulsions of the brain of normal guinea pigs and mice or sterile chick embryo mediums. Cultures from the brains of forty-three guinea pigs and 107 mice. 150 animals, that remained well and that were killed revealed streptococcus in only two instances. From these experiments it was concluded that the streptococcus which we have isolated so consistently was a probable source of virus."

Rosenow attempted to determine whether the streptococcus would invade the brains of animals caused to

breathe, and perhaps to swallow, the streptococcus and, if so, whether the virus could be produced in this way. Pure cultures of streptococci far removed from original sources were nebulized into the air of cages in which mice were kept and were added to running water in which fish were kept. Encephalitis was produced in mice by this means. Moreover, emulsions or filtrates of emulsions of the brains of mice which died of encephalitis, when inoculated through three additional passages in mice, produced encephalitis in significant numbers in the three passages.

Similar experiments were carried out on fish. Emulsions or filtrates of emulsions of the brains of 6 fish, representative of a group dying in large numbers in 1941 during the encephalitis epidemic, produced encephalitis in 11 of 27 guinea pigs and in 22 of 38 mice after intracerebral and intralingual inoculation. Further experiments tended to show that the transmission of the streptococcus was by respiration or ingestion of the streptococcus contained in the water.

"Sections of the brains of the fish died late after exposure to the streptococcus revealed lesions of encephalitis, as did sections of the brains of guinea pigs and mice that were inoculated with emulsions or filtrates of emulsions of the brains of fish and mice that were caused to respire the streptococcus. The lesions became more typical as the virus was passed successively through guinea pigs and mice. Diplococci similar to those found in sections of the brain in studies of epidemic encephalitis in human beings were found in the lesions of some of the animals that died from spontaneous encephalitis and in the lesions of guinea pigs and mice that succumbed to encephalitis after inoculation of virus strains obtained from nature and from experimental animals. A virus phase of the streptococcus appeared to have developed in the mice and fish that were made to respire and perhaps swallow the streptococcus."

Rosenow concludes from his experiments that (1) the streptococcus is a source of what is now considered virus, (2) that virus represents the filtrable phase of the streptococcus and (3) that spread of the streptococcus by air was a major factor in causing encephalitis to occur in epidemic proportion over such a vast area in 1941.

ALPERS, Philadelphia.
[ARCH. NEUROL. & PSYCHIAT.]

HEMOPHILUS INFLUENZAE MENINGITIS IN AN INFANT TREATED WITH SULFATHIAZOLE. DUNCAN LEYS, Brit. J. Child. Dis. **40**:1 (Jan.-March) 1943.

Leys reports the complete recovery of an infant aged 10 months from Haemophilus influenzae meningitis. In all, 74 Gm. of sulfonamide drugs was given during the seven weeks' course of the illness (61 Gm. of sulfathiazole, 8 Gm. of sulfadiazine and 5 Gm. of sulfamethazine). The child had two relapses after use of the drugs was discontinued. Although the condition is designated as "cured," there is no statement as to the length of the follow-up study.

LANGMANN, New York.

Psychology and Psychiatry

IRRESPONSIBILITY OF JUVENILE DELINQUENTS. D. A. THOM, Am. J. Psychiat. **99**:330 (Nov.) 1942.

Thom discusses the group of juvenile nonconformists who are well endowed intellectually and are not suffering from a recognized type of mental illness but who are guilty of serious crime and are considered as incorrigible. As an example, he details the case of a 15 year old boy who since the age of 3 had been a problem child, his offenses becoming increasingly serious and culminating in an atrocious murder. In the report of the psychiatrists who examined this boy, the need was stressed for some rational medical and legal handling of the problem of the constitutional psychopath. Thom points out that the judiciary recognizes only frank mental disease and obvious mental deficiency as mitigating factors. Psychiatrists, on the other hand, have frequently come to consider the psychopath as irresponsible. The necessity for joint action of the legal and the medical forces is obvious.

FORSTER, Philadelphia.
[ARCH. NEUROL. & PSYCHIAT.]

AUTONOMIC NERVOUS SYSTEM FUNCTION IN CHILDREN WITH BEHAVIOR PROBLEMS AS MEASURED BY THE PAROTID SECRETORY RATE. R. S. LOURIE, S. E. BARRERA and E. I. STRONGIN, Am. J. Psychiat. **99**:419 (Nov.) 1942.

Lourie, Barrera and Strongin measured the secretory rate of the parotid gland in children with behavior problems. The method is a measure of the parasympathetic activity. Ninety-seven children with behavior problems were studied; 45 of them had an abnormally high secretory rate. Follow-up studies of the clinical condition from six months to a year later indicated a higher incidence of improvement for those who had normal secretory rates. The authors conclude that while the parotid secretory rate appears to be a criterion of parasympathetic activity in children, it should not be considered an absolute index.

FORSTER, Philadelphia.
[ARCH. NEUROL. & PSYCHIAT.]

THE ETIOLOGY AND THERAPY OF SPASTIC SPEECH. MAURICE H. KROUT, J. Speech Disorders **7**:193 (Sept.) 1942.

Some of the literature on stuttering regarding incidence, theories of causation and symptomatology is surveyed, and some of the methods for treatment are presented. No method is completely successful. The cause of stuttering is not completely known.

PALMER, Wichita, Kan.

STUDIES IN THE PSYCHOLOGY OF STUTTERING: XVII. A STUDY OF THE TRANSFER OF THE ADAPTATION EFFECT IN STUTTERING. WILLIAM E. HARRIS, J. Speech Disorders **7**:209 (Sept.) 1942.

Twenty stutterers read a 180 word passage four times, a similar 180 word passage fifteen times and another 180 word passage four times. Stuttering is reduced as a stutterer rereads the same passage. This reduction apparently also occurs when he reads a new passage similar to the one he has just read several times. This adaptation effect does not extend to conversation.

PALMER, Wichita, Kan.

A STUDY OF THE INFLUENCE OF COMMUNICATIVE RESPONSIBILITY IN A CHORAL SPEECH SITUATION FOR STUTTERERS. JON EISENSON and CHARLOTTE WELLS, J. Speech Disorders **7**:259 (Sept.) 1942.

In a study of 19 stutterers, 9 stutterers read aloud with an individual clinician and then read a similar passage to a hypothetic audience. There apparently was some decrease in the quality of their speech when an actual communication to an audience was requested, but the results were for the most part not mathematically significant.

PALMER, Wichita, Kan.

A Working Hypothesis as to the Nature and Treatment of Stuttering. Julian B. Rotter, J. Speech Disorders **7**:263 (Sept.) 1942.

The early history and a psychologic method of treatment of 8 stutterers is presented. No speech training of any kind was given the stutterers, but a therapy was worked out on the basis that stuttering is a defense mechanism. In 2 cases the condition was completely corrected and in 2 it was very nearly corrected; in the others it was unimproved. The author feels that stuttering is a result of a sensation of inadequacy which is produced entirely exogenously, that pampering is commonly found in the early histories of young stutterers and that the subject's attitude toward stuttering is characteristic of his whole attitude toward life.

Palmer, Wichita, Kan.

Diseases of the Genitourinary Tract

Kidney Infarct. Francisco Laport, J. de pediat. **8**:407 (Sept.-Oct.) 1942.

A baby 2 months old was found at autopsy to have a renal infarct. Review of the literature shows that the disease is rare and that it has always been diagnosed by postmortem examination.

Lozoya S., Mexico, Mexico.

Surgical Intervention for Congenital Malformations of the Genitourinary Tract. Dagmar A. Chaves, Rev. med. munic. **5**:5 and 107 (Jan. and Feb.) 1943.

The author reviews the subject completely under six topics: (1) basic conceptions of plastic surgery, (2) congenital giant hydronephrosis in a child with scrotal hypospadias and bilateral ectopic testicle, (3) testicular ectopia, (4) operative treatment of complete congenital extroversion of the urinary bladder, (5) surgical treatment of epispadias and (6) surgical treatment of hypospadias by Ombedanne's method. These subjects are illustrated with photographs and descriptions of cases from the author's clinical experience. There is a complete bibliography for each subject. This is an excellent review and should be read in full by any one interested in the subject.

Sanford, Chicago.

Diseases of Muscles, Bones, Joints and Lymph Glands

Treatment of Diseases of Muscle. A. T. Milhorat, New York State J. Med. **42**:2210 (Dec. 1) 1942.

Vitamin E (alpha tocopherol) was given to 65 patients, 20 of whom had progressive muscular dystrophy. The average period of treatment was six months, though in some cases it was as long as two years. The dose used was 56 mg., given intramuscularly three times a week. The vitamin was of little or no value.

Ascorbic acid, 200 to 500 mg. daily, caused no improvement in 16 patients with progressive muscular dystrophy, even after many months of treatment. The good results that have been reported by others were probably due to the fact that some patients react favorably when any new substance is tried.

Aikman, Rochester, N. Y.

A Case of Tietze's Disease. G. T. Wrench, J. Indian M. A. **12**:146 (Feb.) 1943.

The author reports a case of Tietze's disease (mildly painful and tender swelling of the costal cartilages, of insidious onset, associated with little or no constitutional disturbance) which involved the seventh, eighth and ninth costal cartilages of the right side, and which persisted for almost six weeks.

Gonce, Madison, Wis.

Diseases of the Eye

Fibroblastic Overgrowth of Persistent Tunica Vasculosa Lentis in Infants Born Prematurely. T. L. Terry, Am. J. Ophth. **25**:1409 (Dec.) 1942.

This is the third of a series of studies on the development and regression of the hyaloid artery and the tunica vasculosa lentis. The material used consisted of serial sections of eyes from more than 50 human fetuses, representing many stages of development. The eyes of fetal and newborn animals, including the cat, rat, pig and opossum, were also studied. The observations and conclusions are summarized.

Reese, Philadelphia. [Arch. Ophth.]

Nutritional Degeneration of the Optic Nerve in Rats: Its Relation to Tryparsamide Amblyopia. Walsh McDermott, Bruce Webster, Richard Baker, James Lockhart and Ralph Tompsett, Pharmacol. & Exper. Therap. **77**:24 (Jan.) 1943.

The toxic reactions of tryparsamide on the optic nerve limit its usefulness in neurosyphilis. Because of the clinical and experimental evidence of the importance of vitamin nutrition in disease of the optic nerve, and particularly because of the evidence of its role in the prevention of toxic damage to nerves, it was felt that an experimental study of tryparsamide from this standpoint would be worth while. Young growing rats of both sexes were used for the study.

The authors' results and conclusions are, in part, as follows: "Rats maintained on synthetic diets lacking only the complete vitamin B complex showed degeneration of the optic nerve. This degeneration was intensified by the concurrent administration of tryparsamide." With the same diet plus brewers' yeast or all the available crystalline B vitamins, there was evidenced no degeneration of the optic nerve, whether or not the animals had received tryparsamide.

In rats maintained on synthetic diets completely free of vitamin A the optic nerves degenerated rapidly. There was no evidence that the administration of tryparsamide intensified this process. The changes in the animals treated with tryparsamide were, if anything, somewhat less evident than those in the untreated animals, but this difference is probably only an apparent one, as the changes were extensive in both groups.

"Rats maintained on synthetic diets supplemented by adequate amounts of B-complex (yeast) and vitamin A (cod liver oil) developed no degeneration of the optic nerve, whether or not they were treated with tryparsamide."

Pilcher, Cleveland.

A Rare Congenital Ocular Abnormality. G. S. Pendse, Indian J. Ophth. **4**:1 (Jan.) 1943.

A girl, born at full term, would not open her eyes at birth, and examination revealed absence of the eyeballs though a bluish swelling within the right orbit showed that the condition was not anophthalmos. Examination a few weeks later showed that the swelling was increasing under the skin, which was bluish, and revealed another swelling in the left lower lid. Transillumination revealed that both were transparent. There

were no other ocular or extraocular abnormalities. The diagnosis of bilateral microphthalmos with cysts, though the most probable one, cannot be verified without pathologic examination of the cysts. The article is illustrated.

ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

Skin Diseases; Allergy

RELATIONSHIP OF THE EOSINOPHIL RESPONSE TO FACTORS INVOLVED IN ANAPHYLAXIS. DAN H. CAMPBELL, J. Infect. Dis. **72**:42 (Jan.-Feb.) 1943.

Histamine, acetylcholine and cysteine, of themselves, are not eosinophilotactic, but they enhance the eosinophilic response in sensitized animals, or in normal animals given a single injection of an antigen such as ascaris keratin.

Substances which diminish or prevent anaphylaxis also diminish or prevent eosinophilia.

The refractoriness of the eosinophilic response to repeated injections of antigen in sensitized animals is due to neutralization of the hypersensitive state and not to depletion of the reserves of eosinophils.

No eosinophilotactic substances could be found in the blood of shocked animals. TOOMEY, Cleveland.

EXPERIMENTAL STUDIES WITH THE DERMATOPHYTES: IV. THE INFLUENCE OF AGE UPON THE ALLERGIC RESPONSE IN EXPERIMENTAL RINGWORM IN THE GUINEA PIG. EDWARD D. DELAMATER, J. Invest. Dermat. **5**:423 (Dec.) 1942.

The differences between the allergic reactions of guinea pigs of different ages during and after ringworm infection were studied. Three age groups were used: newborn animals, medium-aged animals and adult animals. Averages taken of the reactions of each group show that there is a development of the ability to react, from a low level in the newborn to a high level in the adults. Study of the variations met within each group shows that the ability to react allergically develops progressively with age. All newborn animals react in a typical manner with an allergy of low degree. The adult group were found to have acquired generally a higher degree of allergic reactivity. It is concluded that a maturation factor exists in the development of allergy to ringworm infections. The occurrence of the minimal type of allergic response in young animals is considered to offer a basis for explaining the observations that younger animals are more susceptible to progressive ringworm infections than older animals.

BLUEFARB, Chicago. [ARCH. DERMAT. & SYPH.]

ALLERGY IN CHILDHOOD. BERT RATNER, New York State J. Med. **42**:2029 (Nov. 1) 1942.

Asthma may be due to bronchial spasm or to bronchial obstruction, and drugs that help the former may not help the latter. This explains the failure of epinephrine and ephedrine in some cases.

Large amounts of epinephrine may produce bronchiolar constriction and other undesirable results. A child should never be given more than 2 or 3 minims (0.1 to 0.2 cc.) of epinephrine hydrochloride solution (1:1,000); [this dose may be repeated in twenty to thirty minutes]. Administer the drug subcutaneously not intramuscularly. Such repeated small doses are preferred to large doses of epinephrine base in oil. If several small doses do not work, there is no sense in continuing the use of the drug. Epinephrine given by inhalation is dangerous to children and may produce abdominal crises.

Thoughtless use of ephedrine in the nose may cause trouble. When asthma is due to obstruction, Ratner uses syrup of ipecac, ½ to 1 teaspoon. The vomitus should be examined for plugs. Plugs are expelled by three mechanisms: (1) the cough reflex; (2) the action of cilia; (3) a wave action resembling peristalsis. "Tracheal vomiting" releases the obstruction.

The use of morphine in the treatment of patients with asthma is little short of criminal. The value of histamine and histaminase is questioned, and theophylline ethylenediamine has little value in the treatment of children. AIKMAN, Rochester, N. Y.

NAEVUS FLAMMEUS TREATED BY THORIUM X. H. C. SEMON, Proc. Roy. Soc. Med. **36**:44 (Dec.) 1942.

A child 10 years of age had been given gradually increasing doses of thorium X for a large nevus involving the left side of the face. The treatments were given three weeks apart for at least ten months. From the treatment there was no atrophy, but the color became much less conspicuous, chiefly on account of the deposition of brownish pigment which masked the bright tinge of the underlying capillaries.

WILLIAMSON, New Orleans.

PERSISTENT INTERTRIGO? DIAGNOSIS. ALICE CARLETON, Proc. Roy. Soc. Med. **36**:46 (Dec.) 1942.

An infant at 5 weeks of age had otitis externa, first in the left ear and three days later in the right. Soon afterward the natal cleft and the vulva became affected, followed by the anterior right axillary fold, and at 19 weeks the groove between the lower lip and the chin was involved. The affected areas showed a background of bright erythema. In the center of the patch, thick, sodden, white desquamating epidermis was seen. Behind the ears, outside the sodden area, the skin was thin and glazed. If areas were not constantly cleansed they became foul smelling. Investigations and treatment are given in the conclusion of the report.

WILLIAMSON, New Orleans.

ECZEMA AND DERMATITIS. V. PARDO CASTELLÓ and BERTA READ, An. brasil. de dermat. e sif. **17**:7, 1942.

The authors' review of the literature on the present conception of eczema and dermatitis shows the existing confusion in the terminology. A complete study of 209 cases showed that in 74 of them the condition was due to contact, in 20 with soaps, lotions or ointments and in 13 with nail polish. In other cases the condition was due to different causes, including tropical fruits, such as mangos (Manguifera indica) and mamoncillos (Melidia occidentale), and tropical plants, such as guao (Comocladia dentata). In 32 cases dermatitis was produced by internal disturbances; in 22 of these it was cured and in 1 improved. The conditions more commonly encountered were gastric, hepatic, intestinal, diabetic or nervous disturbances.

The authors conclude that it is necessary to return to the conception that eczema and dermatitis are cutaneous reactions due to a number of local or general disturbances, allergy, chiefly by contact, being only one of them. Gastrointestinal and hepatic conditions, cholecystitis, enteritis and colitis are among the most frequent causes of eczema. The clinical entity of infantile eczema should disappear, as probably only 2 per cent of cases of this entity are allergic phenomena of the hereditary and familiar type. The word "atopy,"

according to the authors, should be replaced by idiosyncrasy, or better, allergic idiosyncrasy.

CAÑIZARES, New York.
[ARCH. DERMAT. & SYPH.]

Miscellaneous

A PHARMACOLOGIC STUDY OF EPINEPHRINE SUSPENSIONS IN OIL. RICHARD KOHN RICHARDS, J. Allergy **14**:177 (Jan.) 1943.

The toxicity of an oil suspension of epinephrine base is about equal to that of a freshly prepared aqueous solution of epinephrine hydrochloride when injected intramuscularly in rats. Commercial solutions containing sodium bisulfite have a higher toxicity. There is difficulty in controlling absorption from oil suspensions; toxic symptoms develop, and at times deaths occur, as rapidly as with aqueous solutions. A preparation made of epinephrine which has been triturated, so that the particles are smaller, is less toxic, but also less potent and stable than a preparation made of coarser particles.

HOYER, Cincinnati.

ON THE MODE OF ACTION OF THE SULFONAMIDES: III. PURINES, AMINO ACIDS, PEPTONES AND PANCREAS AS ANTAGONISTS AND POTENTIATORS OF SULFONAMIDE IN E. COLI. HENRY I. KOHN and JEROME S. HARRIS, J. Pharmacol. & Exper. Therap. **77**:1 (Jan.) 1943.

Certain substances, especially peptones, can potentiate or antagonize the action of sulfonamide drugs on Escherichia coli in cultures. At present it seems that in natural conditions the balance always favors the antagonists, as seems to be the case in necrotic processes.

The active substances in commercial peptones in relation to the action of sulfonamide drugs may now be divided into two groups. The first group comprises four amino acids, several purines and possibly para-aminobenzoic acid, and accounts for almost all of the antagonism against sulfanilamide. Against sulfathiazole (and also sulfapyridine and sulfadiazine), however, this first group accounts for almost all of the antagonism only when the inhibition of growth is less than about 65 per cent. At greater inhibitions, a second antagonist (P-2), of great power, is active.

PILCHER, Cleveland.

TOXICITY OF TANNIC ACID. HARRY J. ROBINSON and OTTO E. GRASSLE, J. Pharmacol. & Exper. Therap. **77**:63 (Jan.) 1943.

The investigation was made because tannic acid is used extensively in the treatment of burns. While the acid, in larger doses than seemingly could be absorbed from its use in burns, is toxic to laboratory animals by oral, subcutaneous or intravenous administration, little evidence was adduced that it was toxic when applied to large surgically denuded areas in rats and rabbits; however, in the form of a thick paste, a single application was fatal to white mice. When applied to denuded surfaces in the amounts used on burns, the tannic acid caused no appreciable damage to the liver or kidney.

PILCHER, Cleveland.

TOXICITY AND EFFICACY OF PENICILLIN. HARRY J. ROBINSON, J. Pharmacol. & Exper. Therap. **77**:70 (Jan.) 1943.

Studies were made on mice with penicillin, a relatively impure derivative of Penicillium notatum. The toxic dose of penicillin was about sixty-four times the therapeutic dose as determined by subcutaneous injection.

"On the basis of weight, penicillin appears to be more effective than sulfanilamide and its derivatives in streptococcal, pneumococcal and staphylococcal infections in mice."

PILCHER, Cleveland.

CONCENTRATIONS OF SULFADIAZINE IN HUMAN SALIVA ATTAINED BY CHEWING PARAFFIN CONTAINING SULFADIAZINE. JOHN H. ARNETT, WESLEY W. SPINK, RUTH BOYNTON and SUZANNE AGNEW, Proc. Soc. Exper. Biol. & Med. **52**:54 (Jan.) 1943.

Crystalline sulfadiazine, 0.325 Gm., was incorporated in 1.5 Gm. of paraffin and given to 12 human subjects to chew for two hours. High concentrations (20.6 to 888 mg. of sulfadiazine per hundred cubic centimeters) were found in the saliva, while the level in the blood after one hour varied from 0.0 to 1.48 mg. per hundred cubic centimeters. In another group of 8 patients, also given 0.325 Gm. of sulfadiazine in paraffin, the blood levels at one, three and six hours varied from a trace to 2.36 mg. per hundred cubic centimeters. The therapeutic effect of sulfadiazine in paraffin is being studied in patients with acute pharyngitis and tonsillitis of streptococcic origin.

HANSEN, Minneapolis.

LIVER EXTRACT IN ARSENICAL INTOLERANCE. K. D. LAHIRI, J. Indian M. A. **12**:141 (Feb.) 1943.

In 23 cases of intolerance to arsenic during treatment for acquired syphilis, the excretion of hippuric acid was increased and the symptoms were improved by daily intramuscular injections of liver extract. "It is apparent that liver function in arsenical intolerance is improved by the administration of liver."

GONCE, Madison, Wis.

SULFAMETHAZINE: CLINICAL TRIALS IN CHILDREN. P. A. JENNINGS and W. H. PATTERSON, Lancet **2**: 308 (Sept. 12) 1942.

The therapeutic efficiency of sulfamethazine in a small series of cases of bronchopneumonia and meningococcic meningitis in children was encouraging. It showed the same low toxicity as reported for adult patients. Other advantages over sulfapyridine were easier oral administration and longer intervals between doses.

LANGMANN, New York.

LOCAL APPLICATION OF SULFANILAMIDE TO PERIPHERAL NERVES. W. HOLMES and P. B. MEDAWAR, Lancet **2**:334 (Sept. 19) 1942.

The authors showed that the sciatic nerve of the rabbit was not capable of withstanding saturated solutions of sulfanilamide indefinitely without undergoing interruption of the nerve fibers and wallerian degeneration.

LANGMANN, New York.

News and Comment

GENERAL NEWS

Physicians Certified by American Board of Pediatrics, Inc.—The following physicians were certified as specialists by the American Board of Pediatrics, Inc., after the examinations in New York on Nov. 20 and 21, 1943:

Dr. John A. Askin, Baltimore; Dr. Leo S. Bell, East Orange, N. J. (now in the Army); Dr. Daniel Blitz, Woodmere, N. Y.; Dr. Joseph Caplan, Richmond Hill, N. Y.; Dr. Caroline A. Chandler, Children's Bureau, United States Department of Labor, Washington, D. C.; Dr. Samuel L. Cohen, Brooklyn; Dr. Ira H. Degenhardt, New Brunswick, N. J. (now in the Army); Dr. David Dragutsky, Brooklyn; Dr. Max D. Garber, Rochester, N. Y.; Dr. Theodore M. Ginsburg, Philadelphia; Dr. Louis Edward Goldberg, Newark, N. J.; Dr. Wilson Lyon Grubb, Baltimore; Dr. A. Gerald Heller, Flushing, N. Y.; Dr. Thomas Franklin Henley, New York; Dr. Abraham H. Kantrow, Astoria, N. Y.; Dr. Herman Frederick Kotzen, Reading, Pa.; Dr. Ramon Fernandez Marchante, Santurce, Puerto Rico; Dr. Rafael R. Muniz, New York; Dr. Martha A. O'Malley, Hartford, Conn.; Dr. Louis Platt, Gouverneur, N. Y.; Dr. Edward Press, State Health Department, Charleston, W. Va. (now in the Army); Dr. Martha Katherine Reese, New York; Dr. Benjamin Sachs, Acadia Parish Health Unit, Crowley, La.; Dr. Alex Eugene Schefrin, Passaic, N. J.; Dr. Mollie S. Schildkrout, Forest Hills, N. Y.; Dr. Herman Schneck, New York (now in the Army); Dr. Joseph Frankle Siegel, Boston; Dr. Irving Silverman, Boston (now in the Army); Dr. Dorothy Hutchinson Welker, Chicago; Dr. Samuel J. Werlin, Troy, N. Y.; Dr. Arnold Widerman, Philadelphia (now in the Army); Dr. Gustav Wilens, Torrington, Conn.

The following physicians were certified after the examinations in Cincinnati on December 10 and 11:

Dr. Charles E. Anderson Jr., Shreveport, La. (now in the Army); Dr. John C. S. Battley, Port Huron, Mich.; Dr. A. Robert Bauer, Detroit; Dr. Northrop Beach, Minneapolis; Dr. Warren F. Belknap, Detroit (now in the Army); Dr. Stephen C. Bradley, Terre Haute, Ind.; Dr. Earl W. Brubaker, Lansing, Mich.; Dr. Charles Henry Classen, Rosemont, Pa.; Dr. Karl J. Deissler, Oakland, Calif.; Dr. Maurice Bennett Furlong, Jamestown, N. Y. (now in the Army); Dr. John Paul Gibson, Abilene, Texas; Dr. Ina Morriss Harper, Benton Harbor, Mich.; Dr. Willard Z. Kerman, Chicago (now in the Army); Dr. Harry Leichenger, Chicago; Dr. Lawrence Robert Leviton, Trion, Ga.; Dr. Robert R. Macdonald, Pittsburgh; Dr. Frank L. Menehan, Wichita, Kan.; Dr. Hugo Neuhaus, Freeport, N. Y.; Dr. Frank Church O'Neil, Middletown, Ohio; Dr. Roy Pollack, Palisades Park, N. J. (now in the Army); Dr. Saul J. Robinson, San Francisco (now in the Army); Dr. John O. Rydeen, Norfolk, Va.; Dr. John Richard Schroder, Duluth, Minn. (now in the Army); Dr. Samuel Spector, Ann Arbor, Mich.

The American Board of Pediatrics, Inc.—The dates for the fall examinations have been set. Written examinations will be held locally, under a monitor, on Sept. 22, 1944, and an oral examination, in St. Louis, on November 8 or 9, preceding the annual meeting of the American Academy of Pediatrics and of the Southern Medical Association. Further information regarding these examinations may be procured from the secretary, Dr. C. A. Aldrich, 115½ First Avenue, South West, Rochester, Minn.

PERSONAL NEWS

New Appointments for Dr. Arild E. Hansen.—Dr. Arild E. Hansen, professor of pediatrics at the Medical School of the University of Minnesota, has recently been appointed professor of pediatrics and chairman of the department of pediatrics in the School of Medicine of the University of Texas, at Galveston. He has also been made head of the child health program at the University of the William Buchanan Foundation of Texarkana.

DEATHS

Dr. Walter Lester Carr, one of the most beloved American pediatricians, died at Greenfield, Mass., February 2, at the age of 84 years. His death was due to nephritis and myocarditis. Dr. Carr had long been identified with pediatrics in New York and was one of the pioneer pediatricians in this country. He had served in numerous useful capacities, including that of clinical professor of pediatrics at New York University and Bellevue Medical College. His going means another link severed from the recent past of pediatrics.

Dr. Theodore Carl Hempelmann, for many years regarded as one of the outstanding pediatricians in St. Louis, died recently of cardiac disease.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary-Treasurer: Dr. Charles F. McKhann, University Hospital, Ann Arbor, Mich.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto, Canada.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal, Canada.
Place: Boston. Time: Postponed indefinitely.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

Associação Paulista de Medicina, Section on Pediatrics

President: Dr. Vicente Lara.
First Secretary: Dr. Armando de Arruda Sampaio.
Second Secretary: Dr. Paulo de Barros Franca, Av. Brigadeiro Luiz Antonio 393, 1° Andar, São Paulo, Brazil.

British Paediatric Association

President: Prof. L. G. Parsons, 58 Calthorpe Rd., Five Ways, Birmingham.
Secretary: Dr. Donald Paterson, 27 Devonshire Pl., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Nederlandische Vereeniging voor Kindergeneeskunde

President: Dr. J. H. G. Carstens, Servaasbolwerk 14ª, Utrecht.
Secretary: Dr. R. P. van de Kasteele, Laan van Poot 340,'s Gravenhage.
Place: Different places. Time: Three times a year.

Paediatrický Spolok na Slovensku

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

Palestine Jewish Medical Association, Section of Physicians of Children's Diseases

President: Prof. S. Rosenbaum, 26 Bialkstr., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

Sociedad Cubana de Pediatria

President: Dr. Angel A. Aballí Arellano, 17 No. 609 Vedado, Habana.
Secretary: Dr. Julio G. Cabrera Calderin, Hospital Mercedes L y 21 (Vedado), Box 2430, Habana.
Place: Cátedra de Clinica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

Sociedad Mexicana de Pediatria

President: Dr. Fernando López Clares, 12/a. Medellín 191, Mexico.
Secretary: Dr. Jesus Gómez Pagola, Versalles 64, Mexico.

Sociedad Venezolana de Puericultura y Pediatria

President: Dr. E. Santos Mendoza.
Secretary: Dr. P. Oropeza, Hospital de Niños, Caracas.

Société de Pédiatrie de Paris

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincare, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

Uruguyan Society of Pediatrics

President: Dr. Jose Alberto Praderi, Eduardo Acevedo 1132, Montevideo.
Secretary: Dr. Alfredo Ramon Guerra, Paysandú 824, Montevideo.

NATIONAL

American Medical Association, Scientific Assembly, Section on Pediatrics

Chairman: Dr. Hugh L. Dwyer, 315 Alameda Rd., Kansas City, Mo.
Secretary: Dr. Gilbert J. Levy, 188 S. Bellevue Blvd., Memphis, Tenn.
Place: Chicago. Time: June 12-16, 1944.

American Academy of Pediatrics

President: Dr. Franklin P. Gengenbach, 1850 Gilpin St., Denver, Colo.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

American Hospital Association, Children's Hospital Section

Chairman: Dr. Joelle C. Hiebert, 299 Main St., Lewiston, Maine.
Secretary: Dr. W. Franklin Wood, McLean Hospital, Waverly, Mass.

American Pediatric Society

President: Dr. James L. Gamble, 300 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.

Canadian Society for the Study of Diseases of Children

President: Dr. R. R. Struthers, 906 Drummond Medical Bldg., Montreal.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

Society for Pediatric Research

President: Dr. Joseph A. Johnston, Henry Ford Hospital, Detroit.
Secretary: Dr. Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia.

SECTIONAL

Intermountain Pediatric Society

President: Dr. Eugene Smith, 385–24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

New England Pediatric Society

President: Dr. Warren R. Sisson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. James Marvin Baty, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

North Pacific Pediatric Society

President: Dr. M. L. Bridgeman, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. C. G. Ashley, 833 S. W. 11th Ave., Portland, Ore.

Northwestern Pediatric Society

President: Dr. Arild E. Hansen, University of Minnesota, Minneapolis.
Secretary-Treasurer: Dr. Albert V. Stoesser, 205 W. University Hospital, Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Rocky Mountain Pediatric Society

President: Dr. G. R. Fisher, 23 E. Pikes Peak Ave., Colorado Springs, Colo.
Secretary: Dr. Joseph H. Lyday, 1850 Gilpin St., Denver.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. William Weston Jr., 1428 Lady St., Columbia, S. C.
Secretary. Dr. Angus McBryde, 604 W. Chapel Hill St., Durham, N. C.

STATE

Alabama Pediatric Society

President: Dr. Amas Gipson, 948 Forrest Ave., Gadsen.
Secretary-Treasurer: Dr. Ruth Berrey, 2021–6th Ave. N., Birmingham.

Arizona Pediatric Society

President: Dr. Vivian Tappan, San Clemente, Tucson.
Secretary: Dr. Hilda Kroeger, Arizona State Health Dept. (Maternal and Child Welfare Division), Phoenix.

Arkansas State Pediatric Association

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

California State Medical Society, Section on Pediatrics

Chairman: Dr. William C. Deamer, University of California Hospital, San Francisco.
Secretary: Dr. Charles W. Leach, 2000 Van Ness Ave., San Francisco.

Florida State Pediatric Society

President: Dr. Ludo Von Meysenbug, Box 3356, Daytona Beach.
Secretary: Dr. Robert Blessing, 409 Blount Bldg., Ft. Lauderdale.
Place: Concurrent with state association meeting at time of convention.

Georgia Pediatric Society

President: Dr. T. F. Davenport, 104 Ponce de Leon Ave. N. E., Atlanta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. Edward T. Wakeman, 129 Whitney Ave., New Haven.
Secretary: Dr. Herman Yannet, Southbury Training School, Southbury.
Time: Three meetings a year.

Illinois State Medical Society, Section on Pediatrics

Chairman: Dr. Craig D. Butler, 715 Lake St., Oak Park.
Secretary: Dr. A. J. Fletcher, 139 N. Vermilion, Danville.

Indiana State Pediatric Society

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

Iowa Pediatric Society

President: Dr. Mark L. Floyd, Children's Hospital, Iowa City.
Secretary-Treasurer: Dr. James Dunn, Davenport Bank Bldg., Davenport.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION ON PEDIATRICS

Chairman: Dr. A. Clement Silverman, 608 E. Genesee St., Syracuse.
Secretary: Dr. Albert G. Davis, 307 Gas and Electric Bldg., Utica.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, PEDIATRIC SECTION

Chairman: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary: Dr. P. F. Lucchesi, Philadelphia Hospital, Philadelphia.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Charles F. McKhann, University Hospital, Ann Arbor.
Secretary: Dr. Mark F. Osterlin, Central Michigan Children's Clinic, Traverse City.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. E. W. Hancock, 820 Sharp Bldg., Lincoln.
Secretary-Treasurer: Dr. John M. Thomas, 1102 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NEW HAMPSHIRE PEDIATRIC SOCIETY

President: Dr. MacLean J. Gill, 14 N. State St., Concord.
Secretary-Treasurer: Dr. Ursula G. Sanders, 46 Pleasant St., Concord.
Time: Twice yearly.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Thomas M. Watson, Greenville.
Secretary: Dr. Frederick B. Haar, Greenville.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Ben H. Nicholson, 301 N. W. 12th St., Oklahoma City.
Secretary: Dr. Luvern Hays, 108 W. 6th St., Tulsa.
Place: Oklahoma Club. Time: 6:30 p. m., fourth Friday of each alternate month from September to May, inclusive.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Lonita Boggs, 301 E. Coffee St., Greenville.
Secretary-Treasurer: Dr. Hilla Sheriff, Wade Hampton Office Bldg., Columbia.

TEXAS PEDIATRIC SOCIETY

President: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Edwin A. Harper, 301 Rivermont Ave., Lynchburg.
Secretary: Dr. Emily Gardner, 1100 W. Franklin St., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. Andrew Amick, 1021 Quarrier St., Charleston.
Secretary: Dr. A. A. Shawkey, Professional Bldg., Charleston.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND PEDIATRIC SECTION

Chairman: Dr. J. D. Nourse, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. I. B. Silber, 10465 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. I. Nelles Silverthorne, 170 St. George St., Toronto, Canada.
Secretary: Dr. G. P. Hamblin, 2333 Bloor St. W., Toronto, Canada.

BRONX PEDIATRIC SOCIETY

President: Dr. Harry J. Cohen, 1975 Walton Ave., New York.
Secretary: Dr. Walter Levy, 12 E. 88th St., New York.
Place: Concourse Plaza Hotel, 161st St., and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. Harry A. Naumer, 37–8th Ave., Brooklyn.
Secretary: Dr. Lewis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Granada Hotel. Time: Fourth Wednesday of October, November, February, March and April.

BUFFALO PEDIATRIC SOCIETY

President: Dr. A. Wilmot Jacobsen, 187 Bryant St., Buffalo N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Edward J. Wynkoop, 501 James St., Syracuse.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places:: Various cities in New York. Time: Third Tuesday of April and September.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Heyworth N. Sanford, 952 N. Michigan Ave., Chicago.
Secretary: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, Inclusive.

Cincinnati Pediatric Society

President: Dr. Lloyd K. Felter, 3144 Jefferson Ave., Cincinnati.
Secretary: Dr. T. Selkirk, 3530 Re ding Rd., Cincinnati.
Place: Children's Hospital, Elland Ave., Cincinnati. Time: On call.

Dallas Pediatric Society

President: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas, Texas.
Secretary-Treasurer: Dr. Gladys J. Fashena, 4585 Belfort, Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. Hugh Lewis, Detroit, Mich.
Secretary: Dr. John J. Pollack, 622-26 Maccabees Bldg., Detroit, Mich.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

Fulton County Medical Society, Pediatrics Section (Atlanta, Ga.)

Chairman: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.
Secretary: Dr. Harry Lange, 478 Peachtree St., N. E., Atlanta.
Place: Academy of Medicine, 38 Prescott St. N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. Raymond Cohen, 2300 Caroline St., Houston, Texas.
Secretary: Dr. Betty Moody, 526 Richmond Rd., Houston, Texas.
Place: College Inn, Houston. Time: Fourth Monday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. Edwin H. Schorer, 1103 Grand Ave., Kansas City.
Secretary: Dr. H. E. Petersen, Kirkpatrick Bldg., St. Joseph, Mo.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Oscar Reiss, 2200 W. 3d St., Los Angeles.
Secretary-Treasurer: Dr. Elena Boder, 1830½ Lucille Ave., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Harry Bikoff, 850 St. Marks Ave., Brooklyn.
Secretary: Dr. Henry Rascoff, 895 Eastern Parkway, Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., fourth Monday of each month, October to April, inclusive.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. Meyeron Coe, 217-02-91st Ave., Queens Village, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144-38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. Harry A. Spigel, 2647 Connecticut Ave., Washington, D. C.
Secretary-Treasurer: Dr. Perry W. Gard, 2520 Woodley Rd., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., fourth Thursday of every month.

Memphis Pediatric Society

President: Dr. F. T. Mitchell, 376 S. Bellevue Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

Milwaukee Pediatric Society

President: Dr. John H. Reynolds, 1628 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. F. J. Mellencamp, 324 E. Wisconsin Ave., Milwaukee.
Place: Milwaukee Athletic Club. Time: Second Wednesday of each alternate month, beginning with February.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Edith M. Lincoln, 600 Park Ave., New York.
Secretary: Dr. John D. Lyttle, Babies Hospital, New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northern California Affiliates

President: Dr. Crawford Bost, 490 Post St., San Francisco.
Secretary: Dr. William A. Reilly, 384 Post St., San Francisco.
Time: Second Thursday of September, November, January, March and May.

Oklahoma City Pediatric Society

President: Dr. William M. Taylor, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 625 N. W. 10th St., Oklahoma City.
Place: Oklahoma Club. Time: Third Thursday of each month.

Philadelphia Pediatric Society

President: Dr. Theodore S. Wilder, Greene and Coulter Sts., Germantown, Philadelphia.
Secretary: Dr. Sherman Little, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday in March, May, October and December.

Pittsburgh Pediatric Society

President: Dr. Carl Ruder, 646 Washington Rd., Mount Lebanon, Pittsburgh.

Secretary-Treasurer: Dr. C. J. Stoecklein, 125 De Soto St., Pittsburgh.

Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate month from October to June, inclusive.

Richmond Pediatric Society

President: Dr. Stanley Meade, 913 Floyd Ave., Richmond, Va.

Secretary-Treasurer: Dr. Louise Galvin, 214 S. Boulevard, Richmond, Va.

Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., third Thursday of each month, except June, July and August.

Rochester Pediatric Society

President: Dr. Herbert Soule, 122 Rutgers St., Rochester, N. Y.

Secretary-Treasurer: Dr. Jerome Glaser, 300 S. Goodman St., Rochester, N. Y.

Place: Rochester Academy of Medicine or arrangement by program committee. Time: Third Friday of each month from October to May.

St. Louis Pediatric Society

President: Dr. Jerome Diamond, 508 N. Grand Ave., St. Louis.

Secretary-Treasurer: Dr. Mary A. McLoon, 408 Humboldt Bldg., St. Louis.

Place: St. Louis Medical Society Bldg. Time: First Friday of each month from November to June.

Seattle Pediatric Society

President: Dr. Frederick B. Joy, Stimson Bldg., Seattle.

Secretary: Dr. Sherod M. Billington, Medical Dental Bldg., Seattle.

Place: College Club. Time: Third Friday of each month from September to June at 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Jeanette Harrison, 1136 W. 6th St., Los Angeles.

Secretary: Dr. Henry F. Gallagher, 1930 Wilshire Blvd., Los Angeles.

Place: Jonathan Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Campbell Harvey, 35 W. Huron St., Pontiac, Mich.

Secretary: Dr. Harry A. Towsley, University of Michigan, Department of Pediatrics and Communicable Diseases, Ann Arbor, Mich.

Westchester County Medical Society, Pediatrics Section (New York)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonkers, N. Y.

Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.

Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.